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EVALUATION OF RED CROSS GAMMA GLOBULIN AS A PROPHYLACTIC AGENT FOR POLIOMYELITIS

1. PLAN OF CONTROLLED FIELD TESTS AND RESULTS OF 1951 PILOT STUDY IN UTAH

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The principal purpose of the experiment described in this and subsequent papers of the series was to determine whether gamma globulin, as prepared for and furnished by the American National Red Cross for measles prophylaxis, would protect against the paralytic manifestations of poliomyelitis when administered in reasonable dosage before the onset of illness. A secondary purpose was to determine, if protection were afforded, the duration of protection in the dosage selected for the experiment. From this, based on half life studies of gamma globulin in the childhood age group, the dosage suitable for any period of protection desired could be calculated. Another secondary purpose was to determine whether gamma globulin would permit or interfere with inapparent or milder types of nonparalyzing clinical infection and the subsequent development of active immunity. This question had considerable significance, for if harmless infection and subsequent active immunity were prevented, gamma globulin would have a much more limited field of practical application.

Red Cross gamma globulin was specifically selected for this test because, to our knowledge, it was the only gamma globulin that had been tested for the presence of antibodies to all three types of poliomyelitis virus.[1] Furthermore, all lots tested had shown essentially identical titers. The fact that each lot was prepared from pooled plasma obtained from tens of thousands of donors from many areas of the country furnishes the probable explanation of this uniformity in antibody titer to all three virus types. So far as is known, these criteria have not been applied to other products.

This study appeared to have considerable, immediate importance, since epidemiological studies had led to no hope of control in the near future by breaking the infection chain. Furthermore, no active immunizing agent was available, and no specific therapeutic drug or antibiotic was known, while the incidence of paralytic poliomyelitis appeared to be increasing. Information obtained from animal experiments suggested strongly that human gamma globulin might give temporary protection. It was available in limited quantities and could be produced in much larger amounts. Since the effectiveness of gamma globulin in man could be determined only through actual administration to human beings and since its safety had been previously determined through use in well over one million cases of measles and hepatitis, a human field test under suitably controlled conditions was believed to be indicated.

The importance of the results, if gamma globulin proved to be effective, lay not only in the field of temporary passive protection but in the possibility of its application to passive-active immunization and even to the evaluation of active immunization. If it did not interfere with inapparent infection and the subsequent development of active, relatively permanent immunity, as work in laboratory animals suggested, its widespread use in an epidemic area could be expected to produce immediate immunity of a transient nature, safely supplemented by more permanent, active immunity in the many children who would normally be exposed to natural infection during the epidemic. Stokes and his co-workers had furnished evidence that this apparently was the action of

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Owing to lack of space, acknowledgments to the organizations, employed personnel, and volunteers who participated in the study will appear only in the authors' reprints.

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1. Bodian, D.: Neutralization of Three Immunological Types of Poliomyelitis Virus by Human Gamma Globulin, Proc. Soc. Exper. Biol. & Med. 72:259 (Oct.) 1949.

gamma globulin in infectious hepatitis.[2] Furthermore, gamma globulin in conjunction with the administration of a minute amount of active virus might be used at some time in the future in infants as a relatively safe, passive-active, immunizing procedure. Another possible application would be as an added safety factor in the administration of experimental "inactive" vaccines, which though shown to be safe for administration to laboratory animals, might still be hazardous for man. Still another very important by-product of this study would be the completion of an almost essential step in the evaluation of any vaccine. Should the antitbody level produced by gamma globulin in the dose used for this study afford protection, it would then be known that persons with this or higher blood antibody level would be within the immune range. Any vaccine producing and maintaining such a level or greater in a small sample of children could be accepted as having adequate antigenic properties without being subjected to a tremendous and costly controlled field test to demonstrate protection during a series of epidemics.

REVIEW OF LITERATURE

For many years animal studies have furnished evidence that partial protection against poliomyelitis could be obtained by passive transfer of antibodies previous to inoculation of the virus. Until approximately the last two years, all of these studies in animals have been handicapped primarily by the lack of a more natural or peripheral route of inoculation; the challenge inoculum in almost all instances was given intracerebrally, a route that could well overwhelm any circulating antibodies. A second handicap was the lack of quantitative methods of titrating both antibodies and challenge inoculum, either serum or virus, although under natural conditions the antibodies only can be titrated and ordinarily the infecting dose of virus is probably extremely small. A third handicap was the lack of knowledge concerning the three types of virus and their immunologic differences, which could well have accounted for many of the discrepancies in the laboratory studies.

It is not the purpose of this review to outline the large number of these studies that suffered from these handicaps, since they were covered briefly in a report by one of us (W. M. H.) in 1949.[3] However, certain animal studies since that time have aided in answering two important questions: (1) whether Red Cross gamma globulin would protect when the challenge inoculum was administered by the peripheral route, and (2) whether gamma globulin would prevent the development of active immunity.

Bodian [1] determined the neutralizing properties of Red Cross gamma globulin against the three types of poliomyelitis virus. An approximately equal titer was obtained against each of the three immunologic types of virus.

Rhodes [4] similarly measured the neutralizing properties of gamma globulin from different sources (at least 16% concentration) against the Lansing strain of virus. In these tests the PD_{50} end point of gamma globulin dilution for placental gamma globulin averaged $10^{-3.5}$, while in the Red Cross gamma globulin the PD_{50} titers ranged from $10^{-2.87}$ to $10^{-4.0}$.

Studies on monkeys inoculated intramuscularly and intranasally probably represent a less severe and certainly a more peripheral challenge than intracerebral inoculation. Bodian [5] challenged rhesus monkeys by intramuscular inoculation of all three types of virus (1 ml. of a 10% suspension of virus with titers ranging from $10^{-4.5}$ to 10^{-6}). Gamma globulin was given in doses of 2 ml. per kilogram of body weight in the calf muscles on one side, followed immediately by injection of virus in the opposite calf muscles. Significant protection was observed. In the case of the Leon virus, this amount of gamma globulin gave at least partial protection when administered from two weeks before to three days after injection of the virus. He also tested the protective effect of gamma globulin (10 ml. per kilogram intramuscularly) in six monkeys when it was administered just prior to intranasal inoculation of virus. Results suggesting some partial protection were obtained.

In the same studies Bodian showed that while he obtained no antibody response to a neutralized mixture of active virus and gamma globulin injected intramuscularly, gamma globulin when administered at a different site from the peripheral inoculation of virus did not interfere with the development of antibodies. Bodian also injected Red Cross gamma globulin in doses of 2 ml. to 10 ml. per kilogram of body weight into monkeys to determine how long detectable circulating antibodies remained. After the 2 ml. dose they were detectable for 17 days and after the 10 ml. dose for 6 weeks.

Bloxsom,[6] after the 1948 outbreak in Texas, summarized the cases occurring after an average dose of 2 cc. of commercial gamma globulin had been given to 841 contacts of recognized cases. Only four cases occurred, with onset 1, 2, 3, and 42 days after the injection of gamma globulin. It was suggested that the gamma globulin had been given too late in the incubation period to protect the first three and possibly protection had worn off in the last case.

BACKGROUND AND DEVELOPMENT OF PLAN

Stokes had participated in an encouraging but inconclusive large-scale, human trial of adult whole blood for prophylaxis in the 1932 epidemic in Philadelphia assisted by Wolman, Carpenter and Margolis,[7] and later demonstrated with Henle in 1942 [8] the antibody content

2. Stokes, J., Jr.; Farquhar, J. A.; Drake, M. E.; Capps, R. B.; Ward, C. S., and Kitts, A. W.: Infections Hepatitis: Length of Protection by Immune Serum Globulin (Gamma Globulin) during Epidemics, J. A. M. A. **147**: 714 (Oct. 20) 1951.

3. Hammon, W. McD.: Possibilities of Specific Prevention and Treatment of Poliomyelitis, Pediatrics **6**: 696 (Nov.) 1950.

4. Rhodes, A. J., and Clark, E. M.: Passive Immunity in Poliomyelitis: II. Lansing Antibody Content of Human Gamma Globulin, Proc. Soc. Exper. Biol. & Med. **76**: 379 (Feb.) 1951.

5. Bodian, D.: Experimental Studies on Passive Immunization against Poliomyelitis: I. Protection with Human Gamma Globulin against Intramuscular Inoculation, and Combined Passive and Active Immunization, Am. J. Hyg. **54**: 132 (July) 1951.

6. Bloxsom, A.: Use of Immune Serum Globulin (Human) as Prophylaxis against Poliomyelitis, Texas State J. Med. **75**: 468 (July) 1949.

7. Stokes, J., Jr.; Wolman, I. J.; Carpenter, H. C., and Margolis, J.: Prophylactic Use of Parents' Whole Blood in Anterior Poliomyelitis: Philadelphia Epidemic of 1932, Am. J. Dis. Child. **50**: 581 (Sept.) 1935.

8. Stokes, J., Jr.: The Use of Immune Bodies in the Treatment of Certain Infectious Diseases (Virus and Rickettsial Disease) Caused by Intracellular Parasites, with Emphasis on Need for Diagnostic Criteria of Infection, Yale J. Biol. & Med. **16**: 415 (May) 1944.

of Red Cross gamma globulin against the Lansing strain of poliomyelitis virus in mice. On the basis of these experiences, he formulated a plan for giving gamma globulin in a human test. When unable to obtain support for a large-scale test, and because a few summer camps for children have been known to suffer a relatively high incidence of poliomyelitis, Stokes and T. F. McN. Scott administered Red Cross gamma globulin to 382 of 1,752 children attending 7 summer camps at the beginning of two successive camp seasons (1947 and 1948). Only one paralytic case occurred in the groups in which gamma globulin was not given, and none in the gamma globulin groups.

In 1949 one of us (W. M. H.) was asked to prepare a paper on "Possibilities of Specific Prevention and Treatment of Poliomyelitis."[3] After the necessary review of the literature, he concluded in this presentation that "a well-controlled experiment with gamma globulin would appear to be in order." Shortly thereafter, he began to develop plans for such a controlled test, and undertook to find the necessary financial support. His preliminary presentation of the plan at a special round table conference on gamma globulin of the National Foundation for Infantile Paralysis in February, 1950, failed to obtain general support among a group of outstanding investigators. This group felt that any field test in humans should await further quantitative animal tests and certain limited laboratory tests on man. In March, 1951, after discussion of subsequent animal and human tests, a suggested field trial was formally presented. Many valuable suggestions and criticisms were received that considerably influenced later planning. Although more workers supported the idea that a large-scale field test was in order, the opinion was not unanimous, and a small-scale pilot study received greater support. A committee on immunization* was appointed by the National Foundation for Infantile Paralysis, composed of 11 nationally recognized investigators from leading research laboratories. Additional advisors, representing various medical and public health organizations,† participated in the meetings. At the first meeting of this group on July 6, 1951, the question arose regarding the safety of performing any type of inoculation during a poliomyelitis outbreak, particularly "control" injections of an inert substitute for gamma globulin. It was agreed that such injections were essential for the conduct of a properly controlled test. Extensive discussion was devoted to this problem, and there was finally unanimous agreement that there was no evidence that injection of a rapidly absorbed substance that contained no foreign protein would lead to or localize paralysis. This committee and group of advisors then unanimously endorsed a pilot study for the injection of approximately 5,000 children in the manner outlined in the plan. The pilot study was recommended so that experience in organization and administration might be obtained and, in addition, afford an opportunity to evaluate the response of the public and that of the organized medical profession to this novel type of trial. It was foreseen that the first trial of gamma globulin would render future tests much more difficult, since many physicians and parents would consider gamma globulin of probable value, thus encouraging its indiscriminate use the following year in many epidemic areas. It was agreed by all that a pilot test of approximately 5,000 children would not give a statistically significant answer regarding the effectiveness of gamma globulin.

PLAN OF TEST

The final plans developed for the pilot test will be described in some detail, since essentially the same methods were followed in each of the three studies performed. Furthermore, evaluation of the results rests on a clear understanding of the methods used.

Need for Controls.—For reliable evaluation of results, essentially alternate controls to receive an inert, safe material resembling gamma globulin would be necessary. Only this type of test would withstand critical scientific scrutiny and be accepted universally as a final evaluation. If all volunteers were inoculated with gamma globulin, the uninoculated group could not serve as comparative controls for many reasons. Fear, motivating volunteering, would bring a higher proportion of children from areas or groups known to be most heavily exposed. Economic, social, and racial differences might readily influence response to public clinics. These and other factors would render the two groups dissimilar. Better cooperation in reporting suspected cases would probably occur among the inoculated than the uninoculated, and our own clinicians as well as physicians of the community could not entirely avoid being influenced in making a diagnosis in questionable cases if they knew that the patient had received an injection of gamma globulin. Thus, bias could not be avoided. Furthermore, among those not receiving injections at the clinics, an unknown number might receive injections of gamma globulin from others, so the control group would not be entirely uninoculated, as planned.

Almost every conceivable variation to avoid "control" inoculations was suggested and carefully considered, but had to be ruled out as endangering the success of the test. This was the most debated problem in planning, because

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* Members of the committee were as follows: David Bodian, M.D., The Johns Hopkins University, Baltimore; John F. Enders, Ph.D., The Children's Hospital, Boston; Thomas Francis Jr., M.D., University of Michigan, Ann Arbor, Mich.; William McD. Hammon, M.D., University of Pittsburgh, Pittsburgh; Howard A. Howe, M.D., The Johns Hopkins University, Baltimore; John R. Paul, M.D., Yale University, New Haven, Conn.; Andrew J. Rhodes, M.D., University of Toronto, Toronto, Canada; Albert Sabin, M.D., The Children's Hospital Research Foundation, Cincinnati; Jonas E. Salk, M.D., University of Pittsburgh, Pittsburgh; Joseph E. Smadel, M.D., Army Medical Center, Washington, D. C.; and Thomas B. Turner, M.D., The Johns Hopkins University, Baltimore.

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it introduced a novel approach in evaluating immunization in man. It was readily recalled that, had typhoid and rabies vaccines been originally tested in this manner, years of uncertainty might have been saved and we might not be in our present, unenviable quandary regarding the efficacy of these immunizing procedures after a great many years of routine application. Diphtheria and pertussis vaccines were used many years before their status was accepted. Since our pilot test was planned, a report has been made by an English group of workers describing their use of control inoculations in a study of several types of pertussis vaccine.[9] They indicated their unwillingness to accept the evaluation of pertussis vaccines slowly acquired over many years through less carefully controlled studies.

Selection of Controls.—In order that no member of the team could be biased by a knowledge of what was injected and that no favoritism or yielding to pressures to obtain the active material for selected children could occur, it was decided to arrange a random distribution of all the vials when they were packed and to give each child the first unit of inoculum presenting in the box in order of serial number and packaging. All units would look alike, and the serial number of the label would be the only means of identification. Fifty units of the same size would be packed in a box, 25 of gamma globulin and 25 of control inoculum, all numbered serially as a single series. Selection of gamma globulin and control units for the box would be made when they were packed at the drug house, as one person picked out at random a black or a white ball from a box containing 25 of each, thoroughly mixed. Each box would be packed by the same manner of random selection so that no two would necessarily be alike. To insure an accurate list of serial numbers and contents, two clerks would record them independently as each unit was selected for packing and given a serial number. One of these duplicate records identifying the content of each unit would be kept at the drug firm and one at the headquarters of the National Foundation for Infantile Paralysis until the final diagnosis had been made on all patients. In this way gamma globulin and control groups should be comparable, and no knowledge of the type of agent used could influence the mother, physician, or consultant in reporting, hospitalizing, or making a final diagnosis, or the physical therapist in grading the degree of muscle involvement.

Control Inoculum.—After considering many alternatives, a solution of autoclaved gelatin such as that widely used as a plasma substitute was selected as a control inoculum. It was known to be safe for parenteral injection in very large quantities, contained no whole protein, was nonantigenic, and in proper dilution closely resembled gamma globulin in that it was the same color, was slightly opalescent, and foamed on shaking. At 5 C a 1.5% solution had the same viscosity as gamma globulin.

9. Medical Research Council Investigation: The Prevention of Whooping-Cough by Vaccination, Brit. Med. J. 1: 1463 (June 30) 1951.

Dosage of Gamma Globulin.—Selection of an appropriate dosage of gamma globulin was a difficult problem. We did not believe that dosage requirement in man could be determined by the dose per pound found necessary to protect any laboratory animal from any type of experimentally induced infection. Satisfactory animal experiments must be planned with a dosage capable of producing 30 to 90% paralytic rates in the controls, while natural infection in man leads to less than 1.0% or even 0.1% paralytic rates. In any test to determine the optimal dosage of gamma globulin for man, it would have to be administered during a period of possible normal exposure to infection. Obviously, an arbitrary dosage had to be selected. Since the principal purpose of the test was to determine whether gamma globulin would protect, it would be better to use a dose larger than necessary rather than smaller. Practical considerations limited this to the maximum dose that could be given without producing too much discomfort or disability. It was essential to keep volunteers participating in large numbers over a period of days until thousands had received injections. Therefore, a dose of from 5 to 12 cc. in a single inoculation appeared to be the reasonable maximum for the age group under consideration. More careful planning and calculations led to the selection of three doses: 4, 7, and 11 cc. for weight groups up to 34 lb. (15.4 kg.), 35 to 61 lb. (15.9 to 27.7 kg.), and 62 lb. (28.1 kg.) and over, respectively. These doses would be suitable for most of the children in the age group 2 through 11 years, and would average approximately 0.14 cc. per pound and range from 0.11 to 0.20 cc. per pound. The control inoculum would be administered in comparable amounts.

Safety Clearance of Biologicals.—All biologicals must pass routine sterility and safety tests normally employed by manufacturers of biologicals and must also be tested and approved by the Biologics Control Division of the National Institutes of Health. Gamma globulin should be tested and approved by the Harvard Plasma Fractionation Committee, as well.

Administration of Biologicals.—For rapid handling of thousands of children in one day, with minimal staff, disposable syringes were considered essential. However, investigation soon showed that a disposable syringe to handle volumes up to 11 cc. was not available and would require a considerable period of experiment and development. Therefore, for the pilot test it was decided to use 5 and 10 cc. glass syringes, standard needles, and bottled biologicals, but it was planned to use the disposable equipment subsequently. The assembled syringes would be packed in five layers containing 10 syringes each in stainless steel boxes padded with cotton gauze pads. To ensure safe sterilization, these bulky packages would be autoclaved for four hours at 20 lb. (9.1 kg.) of pressure. Needles would be packaged between gauze in large petri dishes, since no dispensing wheels were made for needles the length of those used for intramuscular injections. In the packages of all equipment to be sterilized, Diack indicators would be distributed liberally. To avoid needle breakage and permit rapid inoculation of the highly vis-

cous material, 18-gage needles were selected for the 11 and 7 cc. dosages and 20-gage needles for the 4 cc. amounts, which would be administered to the smallest children. In order that the needles would not have to be inserted to the hilt, thus permitting easy removal in case of breakage, 2 and 1½ in. (5 and 4 cm.) lengths were selected for the 18 and 20-gage sizes, respectively.

In handling the children, many plans were considered to avoid crowding, to keep family groups isolated, and to facilitate rapid movement of children through the clinics. It was planned to have several inoculation clinics, each with two injection tables. Large auditoriums, schools, and churches would best supply the needed space for comfortable waiting without crowding. Each family group would progress through five stations in order. The parent or guardian would be required to sign a consent form for each child, and the name, address, age, sex, and date of birth would be recorded on a printed 3 by 5 in. record card. The child would then be weighed and the result recorded on the card. After a check of the completeness of these records, the child would be conducted into the inoculation room. These procedures would all be handled by women volunteer workers under the direction of the clinic supervising nurse. Each of two injection tables would be staffed by a physician, a nurse, a volunteer, and the parent. A third nurse would fill a syringe from the suitable size of vial according to the weight of the child. Leaving the vial on the needle, the nurse would record the vial serial number on the child's record card. During this time the table nurse would apply tincture of iodine-U.S.P., to the right buttock. The tincture of iodine would be allowed to dry before being removed with 70% alcohol. Since Faber [10] pointed out the possibility that poliomyelitis virus might be introduced through contaminated skin by a needle puncture, we felt that it would be wise to use a rapidly effective virucidal agent such as tincture of iodine for preparing the skin. Fairly prompt removal with alcohol would tend to prevent burns or sensitivity reactions. The physician would verify the vial number, the dosage-weight selection, initial the record card, discard the empty vial, and make the intramuscular injection in the upper outer quadrant of the right buttock after attempting to withdraw the plunger of the syringe to guard against intravenous inoculation. The child would then receive a lollipop as a reward. The injection table would be covered with roller-paper, which would be changed for each child. Epinephrine and aromatic spirits of ammonia would be available in each clinic for emergency use.

It was planned to give all injections in the right buttock so that it could be determined later whether there was any association between the site of inoculation and the distribution of paralysis in children who attended the clinic and subsequently contracted poliomyelitis.

Estimation of Number to be Injected and Characteristics of an Epidemic Suitable for the Study.—The test should be carried out in an area in which a very severe epidemic of poliomyelitis was in progress. In such an area a maximum number of cases would occur through normal exposure in the group under observation; public interest would encourage volunteer participation and general community support. It should be preferably a small metropolitan community under a single civil administration to facilitate administrative arrangements with official organizations and to minimize travel between clinics and in follow-up of cases.

Although the number to be inoculated in the pilot test was set at approximately 5,000, estimates were made regarding the total size of sample needed and the ages to be included so the first test could be fitted into a pattern for the whole and all be eventually combined to obtain statistically significant results. In order to estimate the numbers required, certain suppositions had to be made. It was postulated that, if gamma globulin reduced the number of cases by at least 50%, it would be considered a useful agent. Since the period of passive protection would be limited, four weeks was selected arbitrarily as the period of observation after injection for obtaining significant numbers of cases.

It was decided that the first step would be to determine how many cases of poliomyelitis would be required in the two test groups to give a statistically significant result. For this purpose we selected the formula shown, which did not require a knowledge of the size of the experi-

$$\frac{A-B}{\sigma} = 2\frac{r_1 - r_2}{\sqrt{\frac{2pq}{\frac{n}{2}}}}$$

mental groups to be inoculated. A equals the number of cases in the control group, B equals the cases in the gamma globulin group, σ equals standard deviation, r_1 equals proportion of total cases expected in group A (0.5), r_2 equals the proportion of total cases observed in group B, p and q both equal 0.5, and n equals

TABLE 1.—*Number of Cases Required for Statistical Significance in the Test Groups*

A*	B†	A + B‡	$\frac{A-B}{\sigma}$	P.
16	8	24	1.64	0.10
20	10	30	1.83	0.07
24	12	36	2.00	0.05
28	14	42	2.16	0.03

* Number of cases of poliomyelitis in control group.
† Number of cases in gamma globulin group.
‡ Total number of cases in both groups.

total number of cases (A and B). Calculations thus would be based on the supposition that, if gamma globulin were ineffective, 50% of all cases observed in the study group would occur in the gamma globulin group and 50% in the control group, since both were originally of equal size and of equal composition and exposure. Using this formula, a series of calculations was made, based on totals of 24, 30, 36, and 42 cases, with 50% reduction in the gamma globulin group, as shown in table 1. It was

10. Faber, H. K.: Postinoculation Poliomyelitis, Pediatrics 7: 300 (Feb.) 1951.

found that minimal statistical significance was obtained with 12 cases in group B and 24 in group A. We, therefore, had to aim for more than 36 cases to determine whether or not protection was afforded. Larger numbers and a longer period of observation would be essential to determine the duration of effect. Since only paralytic cases of poliomyelitis can be accurately diagnosed clinically, these numbers should represent paralytic cases only. In the analysis of final results it was realized that still another supposition would have to be made. In any group of children injected, a portion of these would already be immune and, furthermore, only a portion of the remaining children who were susceptible would be exposed to infection. It must be postulated, therefore, that chance distribution would, on the basis of the method of random selection, afford an equal number of exposed, susceptible children in the group receiving gamma globulin and in the control group.

For economy of effort and materials, it was planned to give the injections only in the age group in which the risk was greatest. In surveying the age distribution in recent epidemics in this country, it was found that in most areas the age group 1 through 12 included 70 to 80% of all paralytic cases. It was not expected that more than 60 to 70% of the parents of children in the selected age group would volunteer to bring their children for injections, even with optimal publicity and public relations.

In selecting an epidemic area that would attain an over-all morbidity rate of 100 per 100,000 or more, it was noted that a reasonably safe prediction could not be made before a rate of 40 had been attained. Allowing approximately a week for transportation of a team and supplies and making all the necessary local arrangements, the peak of the epidemic might have been reached, but in the many epidemic curves studied it was found that the descending curve almost invariably included more cases than the rising portion of the curve. From reviewing a large number of epidemics that had been studied by ourselves and others in various sized populations, it was concluded that 50,000 children should be inoculated to be reasonably certain of obtaining conclusive results based on the suppositions just stated. The pilot test would thus be only one-tenth of the total trial required.

Legal Aspects.—The giving of injections can be construed as practicing medicine, and our team physicians would probably not be licensed in the state where the study would be done. Therefore, no injections would be given without the supervision or participation of a licensed physician. Each clinic was accordingly planned to be under the direction of a member of the local county medical society. This physician would accept legal responsibility for the clinic. Project personnel were to act under his direction and injections by staff physicians would be given only in his presence. It was planned to have the local physicians work in four-hour shifts, with detailed schedules to be arranged by the local medical society.

The consent form to be signed by the parent would be carefully worded with legal assistance. It should explain accurately the purpose and procedure of the study. It would be printed in the newspapers and read over the radio so that all parents could be fully informed and understand what they would sign before coming to the clinic. We were anxious that everyone would understand that half the children would receive control material. The text of the consent form was as follows:

FORM OF CONSENT

I have been informed that Dr. William McD. Hammon, Professor of Epidemiology of the Graduate School of Public Health of the University of Pittsburgh, with the financial support of of the National Foundation for Infantile Paralysis, Inc., and with the cooperation of the..... County, and.....State Health Departments, has inaugurated in..... County, ...a project which aims at the injection of a large number of children for test purposes in connection with the study of Infantile Paralysis and its causes and remedies. For the purpose of that test, it is proposed that a solution of gamma globulin or a solution of specially prepared gelatin be injected into a buttock of each of the children. The method of identifying the substance injected into each child is such that the person administering the injection does not know which one is being used at the time. To assist this project, I hereby consent that either one of the preparations above mentioned may be injected into the buttock of my child

.....
(Name of Child)

Signed: .....
(Father or Mother)

.....
(Relationship to Child)

.....
(City or Town)

Witness:.....

Date:.....

Selection of Area and Approval of Medical and Public Health Groups.—Since the earliest possible release date for the biologicals for the pilot test would obviously be late in August, a list of only northern counties in the United States containing cities of 50,000 to 100,000 population would be prepared and the appropriate state health officers requested to send weekly telegraphic reports of poliomyelitis morbidity. The weekly experience of these counties for the previous 8 to 10 years would be collected and prepared in graphic form to assist in making predictions from the current statistical reports. A local visit would be planned when an incidence approaching 40 per 100,000 was noted during a series of increasing weekly increments in one of these and the previous seasonal pattern of epidemics in the community suggested that a continuing outbreak might be expected. Tentative telephone clearance would then be obtained from the state health department, followed by a personal visit to explain the project. If approved, personal approval would be sought from the president of the state medical society. A visit would then be made to the local area and approval obtained from the local health officer. The president of the local county medical society and other officers or key physicians would then be carefully briefed on the purposes of the study and the procedures and methods involved. If they believed that the members of their society would probably approve and desire to cooperate and participate, a careful analysis of the epidemic would be undertaken.

The preliminary analysis of the epidemic would involve clinical verification of the diagnosis in a sample of cases, an evaluation of the completeness of reporting, and an attempt to determine accurately the number of cases that had occurred each week by date of onset to be certain that the incidence was still rising. An analysis would be made of age distribution and age specific rates calculated on the basis of the best available population data. These would be compared with local data in respect to previous years. All this information would give assurance that a single disease was responsible for the outbreak and that it was typical poliomyelitis, not encephalitis, asceptic meningitis, or some other disease that might closely simulate poliomyelitis from a clinical viewpoint. The age distribution would also serve to permit selection of the most suitable age group to be included in the test.

Civil government officials and civic leaders would be interviewed to assess the likelihood of adequate public response to the project. When satisfied on all these scores, the clinic teams and other personnel would be called for immediate departure from their home by air, and the biologicals would be shipped by appropriate means.

When the decision had been made that the local situation was suitable, the officers of the county medical society would be requested to call an emergency meeting of the total membership within the briefest period of time. To this group a carefully prepared address describing the plan for the field project in full and accurate detail would be presented. Their active endorsement, cooperation, and participation would be requested after fully explaining their legal responsibility. They would be asked to organize a system for recruiting and assigning volunteer physicians to perform the inoculations, assisted by team physicians. A formal vote would be requested after they had been given an opportunity for questions and discussion. Unless the response was enthusiastic and essentially unanimous, we would withdraw and examine another community. In case of approval, we would suggest that a night letter be sent by the secretary or president, at project expense, notifying all absent members of the decision and recommending their cooperation. No news release would be made until these messages could be expected to be in every physician's hands. Every effort would be made until this time to keep the purpose of the visit strictly confidential among the limited group that it was found necessary to contact, so that no embarrassment could come to the medical profession should they believe it unwise to endorse and participate in the project. These total preparations, it was planned, could be completed in four to five days by a team of two or three of the principal investigators.

Publicity and Preparations for the Clinics.—Following selection of a city for a field trial and after obtaining the support of all official agencies and medical groups, a public announcement of the decision would be made. The widest possible local publicity would be desirable at this time. Press and radio releases would be prepared in advance to insure that full and factual information be available. At a special conference of reporters, editors, radio, and television program directors from this city and any nearby larger city with significant local coverage, this material would be released and fully discussed. The date of opening the clinics, their locations, hours of operation, the age group of children to be included, and the estimated closing day of clinics would be announced. So that the scientific aspects and background of the study would be appreciated by the press, radio, and others, we would try to anticipate and answer through previously prepared and mimeographed releases all questions that might arise.

It was believed that since parents were being asked to bring their children for an unusual type of test, every attempt should be made to explain completely all scientific details of the project and to withhold nothing. National publicity would be avoided whenever possible, since it could not contribute to the success of the local study and might hinder subsequent studies in other areas. However, it was realized that wire services would pick up the story, and national publicity could not be avoided. Local leaders of the women's organizations of the community would be approached to recruit a large group of women volunteers to assist in the clinics.

Follow-up Studies.—After completion of the injections, the next phase of the study would be to determine how many cases of poliomyelitis developed in the children who received the injections. At the completion of the epidemic these would be grouped according to the type of injection received. Secondary aims would be (1) to obtain stool specimens and acute and 30-day blood specimens from all persons in whom poliomyelitis developed and household contacts for later laboratory analysis and (2) to conduct a complete epidemiologic study of the entire outbreak. The personnel for this phase would be (1) an experienced clinician to do clinical evaluation during the acute phase for the purpose of making a diagnosis and to collect specimens for laboratory analysis, (2) a skilled physical therapist to assist the clinician by careful evaluation of the muscle involvement of each patient or person suspected of having poliomyelitis at the end of the febrile period and at 30 and 60 days after onset, (3) a trained epidemiologist to collect and evaluate pertinent data, and (4) a secretary to maintain a central office and assist in keeping records.

The assistance of the medical society would be enlisted for this phase, and all physicians would be requested to report cases or suspicious cases of poliomyelitis directly to our follow-up team office. Permission would be requested of the physician for professional members of our follow-up team to examine each patient and visit each family to obtain the necessary data and specimens. Any of the information collected by our team would be available to the family physician upon request, but we would not disclose to nor discuss our findings with the patients. Our examinations would be for the purpose of gathering research data for our records and not for care or treatment of the patient, except by request of the family physician. To insure uniformity in collection and evaluation of all data a series of suitable forms would be prepared.

It would be important in this study to establish an interval between the date of injection and the date of onset

of disease. Therefore, the date of onset would be arbitrarily set as the date of first symptoms that progressed with continued illness to the stage of central nervous system, involvement, or, in case of a biphasic course with an interruption of clinical illness, the date of the second appearance of symptoms. The latter criterion would be adopted to prevent inclusion of preceding, possibly unrelated febrile diseases.

TABLE 2.—*Weekly Incidence by Date of Reporting, Through Aug. 31, 1951, in Utah County, Utah*

Week Ending	City of Provo	Rest of County	Total
6/12/51	0	1	1
7/20/51	3	0	3
7/27/51	4	3	7
8/ 3/51	3	2	5
8/10/51	0	3	3
8/17/51	1	9	10
8/24/51	10	9	19
8/31/51	1	4	5
Total	22	31	53

Cases would be classified as paralytic or nonparalytic. Individual muscle grading would be on the basis of the usual scale of none, trace, fair, poor, good, or normal rating. Final classification of degree of involvement would be made after the 60-day examination. A diagnosis of nonparalytic poliomyelitis would be made only in the presence of positive spinal fluid findings, associated with the typical nonparalytic type of clinical manifestations. However, only paralytic cases would be considered in the final analysis of the results.

The purpose of the laboratory tests would be to determine whether gamma globulin prevented inapparent infection and the development of active immunity. This could be established by looking for virus in the stools of sibling contacts of patients with poliomyelitis, if the siblings had attended the injection clinics, and by testing the acute and convalescent serums of these sibling contacts to determine whether a rise had occurred in specific neutralizing antibody for the strain of virus isolated from the child or the household case of poliomyelitis. The follow-up team would have detailed plans and equipment for collection, packaging, storage, and shipping of these specimens so that they would arrive in the central laboratory in proper condition. Laboratory studies would be done by the tissue culture technique, supplemented when necessary by tests in laboratory animals.

PILOT TEST, UTAH COUNTY, UTAH

Biologicals and Supplies.—After consideration by a special committee, the American National Red Cross allocated enough gamma globulin from lot no. 157 for this controlled test in poliomyelitis. Sterile, 1.5% gelatin, autoclaved under carefully controlled conditions was supplied in liter bottles by the Knox Gelatin Company. Both materials were packaged by the E. R. Squibb & Sons Company in rubber-capped vials containing 4, 7, and 11 cc. quantities all bearing similar labels. Twenty-five of each were distributed in each box of 50 in the random manner described above, and stamped with a single series of numbers that could be used subsequently to identify the contents of each. Since approval and support of the test was not obtained until July 6, 1951, release of the biologicals following packaging could not be obtained until almost the last of August.

Selection of Area.—On the basis of the morbidity reports collected as planned, preliminary visits were made to five areas in late August before one apparently suitable site was tentatively selected. This was Utah County, Utah. Although not ideal, since a whole series of towns distributed along a 40 mile stretch of highway would have to be included to obtain a sufficiently large population, the characteristics of the epidemic and the reaction of the medical and public health personnel and the civic leaders interviewed in the preliminary survey were most satisfactory.

Utah County had a population in 1950 of 80,967. The centrally located city of Provo accounted for 28,899 and the other towns selected totaled 35,968, making a total of 64,867 for the urban population to whom inoculations were made available. A rough estimate of the contiguous, rural population that might contribute volunteers was 7,500, giving a total of approximately 72,400 population.

Through the week ending Aug. 31, 53 cases were reported. Accurate dates of onset could not be obtained for some during the short time available, so cases were tabulated by week of onset as presented in table 2, except that data were then incomplete for the last week. Rates for Provo were at this time 76.1 per 100,000 and for the entire county, 65.5.

A review of monthly incidence by date of onset for 1941 through 1950 showed the greatest number of cases to have occurred in September, closely approached by August. The only epidemic years, 1943 (rate 140.6 per 100,000), 1945 (rate 34.9), and 1949 (rate 65.1), had reached their peaks in August, August, and September, respectively. It appeared from this experience that the peak of the current outbreak should occur in late August or early September. The age distributions for the whole county of the current outbreak and for the previous years 1941-1950 are presented in table 3. It will be noted that the current outbreak was quite similar in age distribution to that of previous years.

TABLE 3.—*Age Distribution of Cases from 1941 Through 1950 and of Cases Reported Through Aug. 31, 1951, in Utah County, Utah*

Age, Yr.	No. of Cases Reported 1941-1950		1951	
<1	5		1	
1	6		1	
2	14		4	
3	19		3	
4	22		6	
5	25	116 = 58%*	4	32 = 60.4%
6	16		7	
7	11		6	
8	9		2	
9	11		3	
10	4		2	
11	10		1	
12	11		1	
13	8		1	
14	5		1	
15-19	11		4	
20-29	8		4	
30+	5		2	
Unknown	6		0	
Total	206		53	

* Percentage with known age.

After considering many factors, it was decided to select the age group 2 through 8 years for this study. As shown in table 3, 60.4% of all cases had fallen in this seven year age span in 1951 and 58% in previous years. In the age group 2 through 8 years there were an estimated 12,500 children within the area from which

TABLE 4.—*Cases of Poliomyelitis by Week of Onset, Complete 1951 Epidemic in Utah County, Utah*

Week Ending	City of Provo	Rest of County	Total
1/ 6/51	0	1	1
5/25/51	1	0	1
7/ 6/51	1	1	2
7/13/51	0	1	1
7/20/51	4	2	6
7/27/51	5	3	8
8/ 3/51	1	6	7
8/10/51	2	14	16
8/17/51	3	4	7
8/24/51	8	5	13
8/31/51	7	6	13
9/ 7/51	1	4	5
9/14/51	1	5	6
9/21/51	0	2	2
9/28/51	0	2	2
10/ 5/51	1	2	3
10/12/51	0	1	1
10/19/51	2	5	7
10/26/51	0	3	3
11/ 2/51	0	2	2
11/ 9/51	1	4	5
11/16/51	0	1	1
11/23/51	1	1	2
11/30/51	2	1	3
12/ 7/51	0	0	0
12/14/51	1	0	1
12/21/51	0	0	0
12/28/51	0	0	0
Total	43	75	118

we might expect to draw. The 5,000 units of inoculum would permit giving injections to just 40% of the group, presumably a reasonable expectation for the turnout of volunteers.

Among cases in 1951 that occurred through Aug. 31, which were reported as paralytic or nonparalytic, only 3 out of 41 (7.3%) were nonparalytic, suggesting strongly that there were more cases in this community than were actually being reported. A decision was reached on Aug. 29, 1951. It was planned to open the clinics on the day after Labor Day (Sept. 4).

Preparations.—On Aug. 30 the problem was presented to a well-attended special meeting of the Utah County Medical Society. The project was accepted unanimously and with unexpected enthusiasm, and the group agreed to arrange a schedule for their organized participation, both in public relations and in clinic work. A telegram announcing the formal action taken was sent that night to every member not present. Physicians with children in the selected age group spontaneously volunteered to bring their children to be injected so as to set an example for the community.

At noon on the day following the meeting with the county medical society, a press and radio conference was held as planned. Interest and active cooperation were immediately obvious. Local women's organizations began immediate participation by scheduling shifts of volunteers for all clinics. A house-to-house canvass by volunteers was organized.

Five clinic sites were selected for the opening day, the majority of which were in Provo. Other sites in small towns were selected and scheduled for one or two days at a time later in the week. It was planned to operate five clinics daily for five or six days or until the supply of biologicals was exhausted. Clinic hours were 9 a. m. to 9 p. m. The Utah County Medical Society took complete charge of organizing local physician participation, and the auxilliary society of the Utah County Medical Society performed a similar function for women volunteers.

Operation of Clinics.—The public attendance at the clinics was so much greater than expected that several changes had to be made at the end of the first day. The house-to-house canvass was called off, since it was obviously unnecessary. Since almost every syringe and needle was used on the first day, instead of half as planned, provisions had to be made to wash, repack, and autoclave all 1,800 every night. The nearest autoclaves of adequate size were in Salt Lake City, nearly 50 miles away.

Instead of running for five or six days as planned, all clinics were closed in three and one-half days, because the supply of biologicals was exhausted. The daily total injections in all clinics were as follows: 1,459, 1,532, 1,418, and 1,359 (one-half day), for a total of 5,768 ‡ or 46% of the 12,500 children estimated to be in this age group in the area reached by the clinics. The excess over 5,000 (the number of vials prepared for the pilot test) was obtained by splitting some excess 11 cc. vials to make a 4 cc. and a 7 cc. dose. Hundreds of people were turned away when the clinics were closed on the fourth day. There were indications that 75 to 90% of the population had planned to participate and would have done so had supplies been adequate. Use of commercial gamma globulin outside this study was insignificant as shown by a survey of pharmacies before and after the injections and by personal reports of physicians and parents.

TABLE 5.—*Cases of Paralytic Poliomyelitis in the Age Group of Two to Eight Years in Utah County, Utah*

Material Injected	Days After Injection 0-28	Days After Injection 29-84	Total	Population	Rate per 100,000
Gamma globulin	0	1	1	2,871 *	34.8
Gelatin	2	3	5	2,860 *	175.0
None	4	8	12	6,800 †	177.0

* See footnote ‡ to text.
† Estimated population.

Results.—Medical complications and reactions following the injections were insignificant. No needles were broken, and no abscesses occurred. A few children fainted a few minutes after inoculation, but they had a history of having done so following previous injections. In one child, urticaria occurred on the right buttock, spreading to the leg a few hours after injection. Several

‡ Thirty-seven children were excluded later for the analysis shown in table 5, and 25 for table 8 because of incompleteness or inaccuracies of recorded vial number or age on record cards.

children were seen by physicians because of fever and malaise one or two days after injection, but in every reported instance the physician found an explanation other than the injection.

The reaction of the public during and after the clinic period was astonishing. The whole community apparently decided that it had been offered an opportunity to participate in a very important project that could do them no harm, and might lead to immediate local benefit and to long-term benefit for many others. The only discontent expressed was in respect to the length of the waiting lines, the crowding (resulting from the unexpected response) and, above all, the fact that thousands were unable to participate because of exhaustion of the biological supplies.

As shown in table 4, the final tabulation by dates of onset showed that the peak of the epidemic in the county had been reached in the week of Aug. 4 to 10, though the incidence remained high till the end of August. In the city of Provo the peak was reached in the week of Aug. 18 to 24. However, a late wave of cases occurred in mid-October and one or more cases a week occurred through November.

TABLE 6.—*Distribution of Paralysis in Cases in Age Group from Two to Eight Years in Utah County, Utah*

Injection Status	Period	Right Leg	Not Right Leg	Total No.	Right Leg, %
Received injections	After clinic	2	4	6	33.3
Did not receive injections	After clinic	9	3	12	75
	Before clinic	27	23	50	34
	Before and after	36	26	62	58

TABLE 7.—*Severity of Paralysis in Age Group Two to Eight Years in Utah County, Utah*

		Degree of Muscle Involvement *				
Injection Status	Period	1	2A	2B	3	Total
Injected.....	After clinic	0	0	6	0	6
Not injected.....	After clinic	0	3	1	8	12
	Before clinic	2	13	24	11	50
	Before and after	2	16	25	19	62

* Grade 1 represents normal muscle power, grade 2A normal to good muscle power, grade 2B good to normal but some fair muscle power, and grade 3 a trace, poor or fair muscle power.

Table 5 shows the number of paralytic cases that occurred in the area considered to be within range of study participation in the age group 2 through 8 years, beginning the day following injection for the group that had received inoculations and the first day of the clinic for the group that did not receive inoculations. As planned, no information as to the type of inoculation was made available to the investigators until after examination and final diagnosis of the patients.

It will be noted in the table that only one case occurred in a child who received gamma globulin, and that, more than four weeks after injection, while five cases occurred in those who received gelatin. These differences lack statistical significance and might have been due to chance alone.

It was encouraging to note, however, that the rate in the gelatin-inoculated group (175 per 100,000) was essentially identical to that in the uninoculated group (177). The numbers are too small to have significance, and the two groups of children were not known to be comparable as regards immune status or exposure, but there was no suggestion here that the inoculation of gelatin had induced any paralysis.

A more valid analysis of this was undertaken by comparing the number of patients with paralytic disease with right leg involvement in the injected and noninjected groups of the same age to see whether the injection had led to any localization. In the noninjected group, the cases occurring in the periods before and after the beginning of clinics were considered separately. As may be seen in table 6, 33.3% of those who had received injections had right leg involvement and 58% of all who had not received injections.

An analysis by degree of paralytic involvement, of injected and noninjected paralytic cases in the same age group, as presented in table 7, gave no indication that among those in whom the disease developed, the severity of paralysis had been affected in any way by the injections. These data supported the earlier conclusion that the children in this study were not being subjected to a special risk through inoculation.

In order to test the random distribution of the two types of inoculation employed in the study, the data on inoculum, sex, and weight were sorted for each variable. The results are presented in table 8. It appears obvious that a satisfactory random distribution was obtained.

One hundred fifty-four blood serums and 104 fecal specimens were collected from 31 patients and 77 contacts. These were frozen and divided equally between the laboratories of two of the investigators (W. M. H. and L. L. C.). Results will be reported in a subsequent paper in this series. A very complete epidemiologic survey was made by Dr. Wehrle. This will appear as a separate paper of the series.

Since an observation from England had been published recently,[11] reporting a single case of possible transmission of homologous serum hepatitis virus in gamma globulin, it was decided to investigate what might have occurred in approximately 2,800 injections of gamma globulin in this study. This was undertaken simply to obtain further evidence respecting American National Red Cross gamma globulin, knowing that to date no homologous serum hepatitits had been attributed to this material. Four months after the clinics were held, return postal cards were sent to the parents of all children who had received injections. A remarkable return was received, which gave complete assurance that no hepatitis had been acquired from the gamma globulin. A more complete report of this and on the effect of gamma globulin on other infectious diseases occurring in the interval of four months will be presented in a separate paper.

11. Cockburn, W. C.; Harrington, J. A.; Zeitlin, R. A.; Morris, D., and Camps, F. E.: Homologous Serum Hepatitis and Measles Prophylaxis, A Report to the Medical Research Council, Brit. Med. J. 2:6 (July 7) 1951.

APPROVAL OF 1952 PROJECT

On Dec. 4, 1951, a report on the pilot test was presented to the immunization committee of the National Foundation for Infantile Paralysis and the advisory group. This first test had been so eminently successful that the committee recommended continuation in 1952 until a significant answer could be obtained. At a meeting of the state and territorial health officers in the spring of 1952, the plan for a continuation of this study was briefly presented and received their approval. Later, somewhat more detailed mimeographed material on the subject was furnished to all state health officers so they would be adequately informed in case an area in their state should be considered for conduct of a trial. A description of these subsequent definitive tests in 1952 is reported in the next paper of this series (see this issue, page 750).

considered of possible additional importance in future studies with vaccines.

A plan for testing gamma globulin was carefully evolved. It was approved by a special committee of nationally recognized scientists and a group of advisors from several national medical and public health organizations. By a method of random selection, half of the children in the study received injections of gamma globulin and the other half injections of a gelatin solution. No one would know at the time which children were controls and which had received gamma globulin. Only after a follow-up period of the length necessary to establish a final diagnosis in each case would the investigators have access to the records identifying the inoculum. The test would be made on a volunteer group in an epidemic area after publicizing of a full and detailed explanation of the plan to use controls. It was estimated that approximately 50,000 children would have to be included in the study to insure statistically significant results.

TABLE 8.—*Distribution of Gamma Globulin and Gelatin Inoculations by Sex and by Five-Pound Weight Groups*

	Male			Female			Both Sexes		
Weight, Lb.	Gamma Globulin	Gelatin	Total	Gamma Globulin	Gelatin	Total	Gamma Globulin	Gelatin	Total
20-24	6	10	16	35	24	59	41	34	75
25-29	92	99	191	146	127	273	238	226	464
30-34	265	272	537	277	273	550	542	545	1,087
35-39	210	213	423	234	237	471	444	450	894
40-44	245	249	494	229	214	443	474	463	937
45-49	141	194	335	173	146	319	314	340	654
50-54	192	182	374	146	156	302	338	338	676
55-59	133	93	226	91	94	185	224	187	411
60-64	79	85	164	65	73	138	144	158	302
65-69	31	34	65	21	24	45	52	58	110
70-74	14	23	37	15	14	29	29	37	66
75-79	6	6	12	7	7	14	13	13	26
80-84	2	3	5	10	4	14	12	7	19
85-89	2	3	5	5	2	7	7	5	12
90-94	1	2	3	0	1	1	1	3	4
95-99	0	0	0	0	2	2	0	2	2
100-104	0	1	1	1	0	1	1	1	2
105-109	0	1	1	0	0	0	0	1	1
Total	1,419	1,470	2,889	1,455	1,398	2,853	2,874	2,868	5,742 *
Mean Weight, lb.	44.35	44.30		42.55	42.90				
Standard Deviation	11.35	11.80		12.05	11.85				
Standard Deviation of Mean	0.302	0.308		0.316	0.317				

* See footnote ‡ to text.

SUMMARY

On the basis of evidence from experience with laboratory animals, passive prophylaxis of human poliomyelitis appeared theroretically feasible. Human gamma globulin from the American National Red Cross, prepared from large donor pools of plasma collected from extended geographical areas, had been shown to have an equal titer of antibody for all three known types of virus. Since it was known to be safe from extensive use in measles prophylaxis, it was selected as the most suitable form of antibody to be administered in a controlled, human field trial to determine the value of passive immunization against poliomyelitis.

The primary purpose of the test was to determine whether gamma globulin given in reasonable dosage before the onset of the naturally acquired disease, would prevent paralysis. Other questions that it was hoped might be answered concerned the duration of protection, if any, and the development of inapparent infection, with subsequent active immunity. The results of the tests were

According to this plan a pilot study was performed during an epidemic in Utah in September, 1951, during which 5,767 children received injections. The medical and public health professions at the state and local level approved the project before it was presented to the public, and cooperated and participated enthusiastically in carrying out the study. The public response was phenomenal as regards cooperation and participation. There were no serious difficulties encountered in carrying out the study as planned. No significant clinical reactions of any type were observed. There was no evidence that the inoculations led to any increase or localization of paralysis.

As anticipated, the number of cases of poliomyelitis occurring in the injected group was too small to determine whether gamma globulin had afforded any protection. Plans called for continuation on a much larger scale in 1952 in order to obtain significant results.

EVALUATION OF RED CROSS GAMMA GLOBULIN AS A PROPHYLACTIC AGENT FOR POLIOMYELITIS

2. CONDUCT AND EARLY FOLLOW-UP OF 1952 TEXAS AND IOWA-NEBRASKA STUDIES

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As a result of experience in the 1951 pilot test in Utah (see this issue, page 739), in which 5,767 children were injected with either gamma globulin or gelatin during a poliomyelitis epidemic, several minor changes in the original plan were proposed for the continuation studies. The following changes were the more important ones. Through arrangements with the Becton-Dickinson Company, a disposable syringe with a preloaded cartridge containing 4, 7, or 11 cc. was perfected. This would allow for much faster operation of the clinics. These syringe units of gamma globulin or gelatin would be assembled and packaged in random order and given serial numbers for identification in the same way as the vial units used in Utah. The label bearing the serial number would be slipped into the extra length of the glass cartridge in the disposable unit and not affixed with adhesive. This label would be removed by the physician and stapled to the child's record. The number would also be written on the record card to avoid the loss of the number if the label were torn off. The written number would later be checked by two separate volunteers to detect any inaccuracy or illegibility. This would provide a much better safeguard against error than the method used the previous year. Since it was more practical to handle the biologicals at room temperature than at 5 C (41 F), the gelatin solution concentration would be increased from 1.5 to 6% to match the viscosity of gamma globulin at room temperature. A lay administrator and a director of women's volunteers would be added to the team.

More thought was given to the importance of determining the duration of any possible effect of gamma globulin. It was realized that if this material was shown to be effective, any later trials with suitable controls to determine the duration of effect of one dose, or the optimal dose for any particular set of circumstances would be almost impossible to perform. It seemed wise therefore to plan to obtain maximal numbers while possible to determine with some accuracy the extent of time during which the selected dose gave protection. On the basis of half-life studies on gamma globulin, a suitable dose could then be calculated for any desired duration of protection.

Dixon, Talmage, and Maurer [2] have provided data for computing the half-life of globulin or gamma globulin in several species of animals. They found the half-life of gamma globulin to be 12 to 14 days in adult man, longer in children, and still longer in infants. In the age groups used in our tests, the half-life appeared to be about 21 days. These data on half-life can be interpreted to mean that if the dose now used in the field tests (averaging 0.14 cc. per pound of body weight) gives protection for four weeks, doubling the dose would extend the protection for an extra three weeks, making a total of 7 weeks' protection; or if the present dose gives protection for six weeks, doubling the dose would extend it for three more weeks for a total of nine weeks' protection. Thus, protection by even a single injection could theoretically be extended for many months, provided there were no limitations to the availability of the agent or the volume that could be injected.

In regard to general procedure for 1952, it was believed that by injecting 50,000 to 60,000 children there probably would be from 50 to 100 paralytic cases in the study group. It seemed possible to accomplish this in three to five epidemic areas. To have at least one, long-continuing epidemic to afford evidence on the duration of protection, one or more southern areas would be selected in which epidemics might begin in May or June and continue through November or December. Three advance teams would be organized to survey and select suitable areas. They would be sent to areas chosen on the basis of statistical data received weekly from 300 counties and background data compiled by F. M. Hemphill of the University of Michigan.

The problem of encountering significant use of gamma globulin by private physicians as a result of the publicity given to the pilot test and to the encouraging reports of laboratory tests gave us real concern. The following final evaluation of the situation as it might affect the 1952 tests was made. The American Red Cross would not authorize the release of any gamma globulin for use in poliomyelitis except to our group, so this source was not to be feared. It was felt that the supply of commercial material was limited and might become exhausted if a heavy call occurred early during the season. If it were available, use by private physicians would reduce to some degree the number of children coming to the clinics, but it seemed unlikely that any significant number would receive it after clinic attendance. Chance would distribute these equally between the gelatin and gamma globulin

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From the Department of Epidemiology and Microbiology, Graduate School of Public Health, University of Pittsburgh; Director of Project and Professor and Head of Department of Epidemiology and Microbiology (Dr. Hammon); Deputy Director of Project and Director, Camden Municipal Hospital for Contagious Diseases and Department of Pediatrics, School of Medicine, University of Pennsylvania (Dr. Coriell); Consultant of Project and Physician-in-Chief, The Children's Hospital of Philadelphia and Department of Pediatrics, School of Medicine, University of Pennsylvania (Dr. Stokes).

1. Deleted on proof.

2. Dixon, F. J.; Talmage, D., and Maurer, P. H.: Half-Life of Homologous Gamma Globulin (Antibody) Molecules in Man, Dog, Rabbit, Guinea Pig and Mouse, Federation Proc. 11(part 1): 466 (March) 1952.

groups, so there would be no serious interference with an analysis based strictly on cases of diagnosed poliomyelitis.

OTHER STUDIES OF USE OF GAMMA GLOBULIN

In the interval since the planning of the pilot test, Adams and co-workers [3] tested the effect of gamma globulin on cynomolgus monkeys fed Y-SK virus (type 2) after tonsillectomy. Half the animals were given 1 or 2 cc. of gamma globulin per pound of body weight and the others served as unprotected controls. No significant differences were noted in the paralytic rates of the two groups. The gamma globulin did not appear to interfere with the development of antibodies after infection.

Horstmann [4] and Bodian,[5] independently, fed virus to cynomolgus monkeys and chimpanzees and subsequently were able to demonstrate viremia in some. The viremia preceded the onset of clinical disease whenever noted in an animal in which paralysis developed. They suggested that viremia may occur during the incubation period of the natural disease in man. Bodian, furthermore, showed that in animals infected by oral administration of virus development of the paralytic disease could be prevented by the injection of much smaller amounts of Red Cross gamma globulin than those previously required for protection against intracerebral or intramuscular inoculations of virus. A low level of antibody apparently prevented viremia. He also noted that gamma globulin in the quantities administered did not prevent excretion of virus in the feces or the development of antibodies as a result of inapparent infection.

TABLE 1.—*Weekly Incidence of Poliomyelitis by Date of Reporting in Harris County, Texas*

Week Ending	Houston	Rest of County	Total
1/ 5/52	0	0	0
1/12/52	3	3	6
1/19/52	2	0	2
1/26/52	2	4	6
2/ 2/52	6	1	7
2/ 9/52	1	0	1
2/16/52	2	1	3
2/23/52	5	1	6
3/ 1/52	1	5	6
3/ 8/52	1	2	3
3/15/52	1	2	3
3/22/52	2	1	3
3/29/52	1	1	2
4/ 5/52	2	0	2
4/12/52	1	1	2
4/19/52	2	1	3
4/26/52	4	0	4
5/ 3/52	8	3	11
5/10/52	4	0	4
5/17/52	3	2	5
5/24/52	1	0	1
5/31/52	8	2	10
6/ 7/52	11	12	23
6/14/52	22	11	33
6/21/52	26	23	49
6/26/52	24	16	40
Total	143	92	235

Hammon, Cheever, and Sather,[6] using suckling mice inoculated intraperitoneally with suckling mouse-adapted MEF1 virus (type 2), found that small doses of Red Cross gamma globulin would prevent paralysis, whereas much larger doses had been required to prevent disease resulting from intracerebral injection. Significant protection was detectable with amounts of gamma globulin as small as 0.05 cc. per pound of body weight, and it was almost complete with 0.1 cc. per pound. These same doses did not prevent the development of active immunity, through inapparent infection, against the subsequent inoculation of Lansing virus. These effective quantities were slightly smaller than those employed in the human field tests. Subsequently, in tests as yet unreported, attempts were made to detect viremia preceding the onset of clinical disease in the suckling mice. No viremia could be detected, so it cannot be concluded at present that the small amount of gamma globulin that interfered with the development of the disease in the mice did so by preventing viremia as an essential stage leading to invasion of the central nervous system.

TABLE 2.—*Age Distribution of Patients with Poliomyelitis Reported in Harris County, Texas, Through June 26, 1952*

Age, Yr.	No. of Cases Reported: Houston		Rest of County		Total	
0	6		6		12	
1	16		9		25	
2	10		11		21	
3	8	63 =	8	52 =	16	115 =
4	8	44%	6	56.5%	14	49%
5	14		10		24	
6	7		8		15	
7	6		6		12	
8	6		2		8	
9	8		..		8	
10	5		3		8	
11	4		6		10	
12	3		2		5	
13	1		4		5	
14	2		..		2	
15-19	9		1		10	
20-29	19		6		25	
30 and over	11		4		15	
Total	143		92		235	

A report published more recently by Wood, Clark, McKendry, and Rhodes [7] is of particular interest. American Red Cross gamma globulin, in doses varying from 0.1 to 0.4 cc. per pound of body weight (which includes the range with which our field tests were concerned) were injected intramuscularly in six children and four adults previously found to have no detectable antibody to Lansing strain virus (type 2). Antibody was then demonstrated in small amounts in the serums of these persons and persisted in a few at a detectable level for several

3. Adams, J. M., and others: Experimental Poliomyelitis: Use of Human Gamma Globulin in Tonsillectomized Monkeys, Laryngoscope **61**: 1010 (Oct.) 1951.

4. Horstmann, D. M.: Poliomyelitis Virus in the Blood of Orally Infected Monkeys and Chimpanzees, Federation Proc. **11**(part 1): 471 (March) 1952; Poliomyelitis Virus in Blood of Orally Infected Monkeys and Chimpanzees, Proc. Soc. Exper. Biol. & Med. **79**: 417 (March) 1952.

5. Bodian, D.: Pathogenesis of Poliomyelitis in Normal and Passively Immunized Primates after Virus Feeding, Federation Proc. **11**(part 1): 462 (March) 1952; Experimental Studies on Passive Immunizations against Poliomyelitis: The Prophylactic Effect of Human Gamma Globulin on Paralytic Poliomyelitis in Cynomolgus Monkeys after Virus Feeding, Am. J. Hyg. **56**: 78 (July) 1952.

6. Hammon, W. McD.; Cheever, F. S., and Sather, G. E.: Gamma Globulin Passive Protection Tests in Mice Injected Intraperitoneally with MEF1 Poliomyelitis Virus, Proc. Soc. Exper. Biol. & Med. **80**: 150 (May) 1952.

7. Wood, W.; Clark, E. M.; McKendry, J. B. J., and Rhodes, A. J.: Studies on Passive Immunity in Poliomyelitis: Lansing Antibody Levels in Humans after Gamma Globulin Administration, Proc. Soc. Exper. Biol. & Med. **80**: 522 (July) 1952.

weeks. At any time, the antibody could be detected only by testing undiluted serum and thus at no time was present at much more than a minimal detectable level. Knowing that these tests were being made, no attempt was made to follow the pattern of antibody loss in any of the children who received injections in our clinics.

HARRIS COUNTY, TEXAS, TEST

Selection of Area.—By late June no suitable epidemic had been found in a community of the predetermined size; however, in Houston and the surrounding Harris County, Texas, what appeared might be an epidemic of greater proportions than any this combined area had experienced previously was developing. Since it had been the weekly number of cases had been increasing constantly, at least until about one week before the current week. The age distribution, given in table 2, indicated that about 50% of all cases were occurring in children in the age group 1 through 6 years. During the previous six years, the only period for which the ages of all patients were available, the age distribution had been essentially the same, 49.6% of the cases occurring in persons in this six year age span. The age specific rates by June 26 (table 3) were already 93 per 100,000 in this age group, while the age specific rates for all other ages was only 16.

As a means of predicting what might be expected for the remainder of the epidemic, the monthly incidence for

TABLE 3.—*Selected Age Specific Incidence and Rate per 100,000 Population of Poliomyelitis Reported Through June 26, 1952, in Harris County, Texas*

Age, Yr.	Houston			Rest of County			Total		
	Estimated Population	No. of Cases	Rate	Estimated Population	No. of Cases	Rate	Estimated Population	No. of Cases	Rate
1	15,811	16	101	6,085	9	148	21,896	25	114
2	14,372	10	70	5,810	11	190	20,184	21	104
3	15,167	8	53	6,396	8	125	21,563	16	74
4	14,642	8	55	6,422	6	94	21,064	14	66
5	13,807	14	101	6,113	10	164	19,920	24	120
6	12,901	7	54	6,055	8	132	18,956	15	79
Total, 1-6 Years	86,700	63	73	36,917	52	141	123,583	115	93
Total, Other Ages	553,300	80	14	197,083	40	20	750,417	120	16
Total	640,000	143	22	234,000	92	39	874,000	235	27

TABLE 4.—*Annual Poliomyelitis Incidence by Months and Annual Rates per 100,000 Population, 1942-1951, in Harris County, Texas*

Year	Population	No. of Cases													Rate
		Jan.	Feb.	March	April	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	Total	
1942	575,500	0	0	0	0	1	1	0	0	1	1	1	1	6	1.0
1943	690,400	1	3	4	1	2	25	46†	21	26	8	5	0	142	23.6
1944	626,300	2	1	1	1	0	1	6	2	7	6	3	1	31	4.9
1945	653,300	1	0	4	2	8	56†	44	32	31	18	6	4	206	31.5
1946	681,500	3	0	3	1	1	18	14	8	13	11	31†	8	114	16.7
1947	710,900	6	1	2	4	2	2	4	4	1	1	4	1	32	4.5
1948	741,500	0	0	0	2	59	96†	79	48	19	9	1	2	315	42.5
1949	773,400	9	0	3	6	1	14	41†	40	30	27	20	8	199	25.7
1950	806,701 *	9	13	13	9	5	18	58	66†	62	40	17	10	320	39.7
1951	841,400	10	4	2	5	11	42	30	40	50†	26	30	17	267	31.7
Total Cases	.....	41	22	32	31	90	273	322	261	240	147	121	52	1,632	...

* Census figure. † Peak month of a year of high incidence.

decided to select one or more outbreaks in a southern area that would give promise of continuing for six months or longer, it was decided to consider whether this outbreak in a population of almost 900,000 persons could be utilized.

Houston, by 1952 estimates, had a population of 640,000, and the remainder of the county had 234,000, a total of 874,000. Most of the county population was in the greater Houston metropolitan area. On June 26, 143 cases had been reported from the city (rate of 22 per 100,000) and 92 from the rest of the county (rate of 39 per 100,000), making a total of 235 cases (rate of 27 per 100,000), as shown in table 1. These cases are tabulated by week of reporting, since the onset date had not been determined for most of the more recent cases. The average delay in reporting for cases with known onset date was seven days. It appeared, therefore, that the past 10 years was reviewed (table 4). During the seven years with annual morbidity rates of 16 per 100,000 or above, the average duration of the outbreak had been about five or six months. On the basis of this evidence, we felt that a sufficient number of cases would occur during the succeeding several months to make this epidemic especially useful for determining the possible duration of protection. The estimated population between the ages of 1 and 6 was 123,583. It was decided to allocate 35,000 units of the biologicals for this group. This meant offering inoculations to about 28% of these children.

Verification of clinical diagnosis on a suitable sample was considered unnecessary, except by interview with a few select physicians. A rough tabulation of cases as reported by type of involvement indicated that 59% were paralytic and 41% nonparalytic; however, despite

this high proportion of nonparalytic cases, it was readily determined from several sources of information that reporting was incomplete, even for paralytic cases.

Preparations.—With eight clinics we considered it possible to inject 35,000 children in 10 or 11 days, but we were prepared to establish only five clinics. Because of the cooperation of the medical schools and hospitals in Galveston, Houston, and Dallas, the necessary additional staff for eight clinics was recruited. Equipment was available locally. On June 25, the executive board of the Harris County Medical Society considered the plan carefully. It was enthusiastically and unanimously endorsed; however, a provision of their bylaws requiring seven days notice for a society meeting made it impossible to present the plan to the total membership. A mimeographed copy of the address that had been prepared was mailed to all members. A telegraphic night letter was sent to all members by the president, informing them that the executive board had approved the plan and urging them to participate and cooperate. On the following day, approval was obtained from all civil and local public health authorities. A press, radio, and television conference was held on Friday, June 27. Women volunteers were organized efficiently by calling for a meeting of the presidents of all women's clubs in the city. Thousands of volunteers were soon recruited and briefed. Clinic sites were selected in areas of greatest population density, both inside and outside the city. Many of these were moved from time to time to afford access to other areas of population.

Operation of Clinics.—Clinics were kept open daily from July 2 through July 12 and for a half day Sunday, July 6, a total of 10½ days. This period covered a three day Fourth of July weekend during which a large portion of the population was out of town. The daily total injections in all clinics were as follows: 2,880; 2,528; 2,443; 1,755; 2,890; 3,272; 3,342; 4,499; 4,769; and 1,691, for a total of 33,137 or 26.8% of the total population between the ages of 1 and 6. Of the injected children, 25,815 (77.9%) were white and 7,322 (22.1%) were Negro. This parallels closely the county's population distribution of 81.4% white and 18.6% Negro. Clinic attendance by Harris County physicians could not have been better. In a number of clinics, additional physicians were recruited on short notice to help care for a heavy load of patients. At times, as many as five physicians were giving injections in a single clinic. By this means, crowding and a long waiting line were quickly remedied.

Local Gamma Globulin Problem.—A few physicians in Houston had been giving prophylactic gamma globulin to normal children for the prevention of poliomyelitis for several years since the report of its use by Bloxsom in 1948,[8] and small doses (1 to 2 cc.) were often given to contacts of patients. Hospital records showed that some physicians were giving large doses for therapy. A survey of the 368 druggists in the city showed that sales of gamma globulin for the entire month of June were 1,260 cc., and in the first five days of July about 14,700 cc. were sold, with two of the largest distributors not reporting. Partial reports for the whole month of July gave a total of 21,976 cc. This, plus the fact that large commercial stocks were found to be available in Houston and in the hands of the regional distributors, was at first felt to be cause for concern. During the period of the study, however, most physicians did not give it to children in the 1 to 6 year age group, and the children who had already received injections from their physicians did not attend the clinics. Furthermore, it was felt that the rare instances of use on sibling contacts who had attended the clinics would not alter the statistical distribution of cases.

Results.—The 33,137 patients receiving injections were slightly short of the 35,000 goal, but it did not seem wise to keep the clinics open over another weekend. Fatigue among the personnel had become acute, and the supply of 4 cc. syringe sizes brought to the area was exhausted. No needles had broken, and no abscesses occurred. Four children had immediate reactions. In two it was characterized by collapse, rapid pulse rate, shallow respiration, and pallor. In another it began with coughing followed by edema of the face and later generalized urticaria. This child had experienced similar reactions before, and the parents were little concerned. The fourth child became comatose and cyanotic and had a generalized convulsion while still on the injection table. He responded promptly to subcutaneously administered adrenalin and, after a short rest, walked away feeling fine. Physicians reported to us another 10 children in whom delayed urticaria developed within 12 to 24 hours after attending the clinics.

TABLE 5.—*Cases of Poliomyelitis in Harris County, Texas, in the Age Groups 1-6 Years, from July 2 to August 26, 1952, According to Week of Onset*

Week Ending	Paralytic	Nonparalytic	Total
7/ 5/52	12	3	15
7/12/52	15	0	15
7/19/52	20	2	22
7/26/52	19	2	21
8/ 2/52	10	0	10
8/ 9/52	11	1	12
8/16/52	8	2	10
8/23/52	4	3	7
8/30/52*	2	1	3
Total	101	14	115

* Data for this week are incomplete, because data were collected through August 26 only.

Just as the number of clinics had to be increased, so the follow-up team previously planned for a smaller city was found to be inadequate. The follow-up team for all of Harris County was composed of one epidemiologist-director, three clinicians, two physical therapists, and two secretaries.

Cases continued to occur throughout the month of July at about the peak rate attained by the middle of June but began to decrease significantly during August. Table 5 shows the morbidity by week of onset in the selected age group (1 through 6 years) from July 2 through August 26, the latest information available at

8. Bloxsom, A.: Use of Immune Serum Globulin (Human) as Prophylaxis against Poliomyelitis, Texas State J. Med. 45: 468 (July) 1949.

the time of writing. During this period of about two months, 115 cases occurred, a rate of 93.1 per 100,000. Diagnosis in some of these cases is still tentative. The only nonparalytic cases included (14 or 12.2% of the total) were those with demonstrated spinal fluid changes. Seventeen (14.8%) cases were of the bulbar or bulbospinal types. Twenty-seven cases occurred in the clinic injected group. Evidence based on the proportion of cases in the clinic (injected) and nonclinic (not injected) groups that were reported directly to us by physicians and not reported to the health departments suggests that our records are much more complete for the clinic group. Thus, as anticipated, no valid comparison of incidence can be made. The control group of children injected with gelatin will be essential in making the evaluation. The type of inoculum received by individual patients has not been determined to date. This information alone will furnish evidence of whether any protection has been afforded by the gamma globulin.

WOODBURY COUNTY, IOWA, AND DAKOTA COUNTY, NEBRASKA, TESTS

Selection of Area.—An advance team visiting Sioux City, Iowa, as the Texas clinics were being closed found it simple to make a positive decision on the suitability of the epidemic, the characteristics of the area, and the cooperation of the population. There could be no doubt that a very large number of cases would occur within the next few weeks. Sioux City and South Sioux City are contiguous areas, separated only by a river but lying in two different states. Since the population just outside of the city limits was of a significant size, it was decided to include the counties in which each city was located. As the counties contained no other urban areas with a population even as high as 1,000, it was determined to establish clinics only in or near these two cities. Sioux City and Woodbury County, Iowa, had an exceedingly stable population, which had shown no significant change from the 1940 census in the 1950 census, so 1950 figures were used for 1952. Sioux City's population was 83,991, the rest of Woodbury County, 19,926, and the total county population 103,917. The population of South Sioux City was increasing, while that of the rest of Dakota County, Nebraska, was decreasing, so estimates were made. The total county population was estimated at 10,514 for 1952. For the two county area the total population was 114,431.

TABLE 6.—*Weekly Incidence by Date of Reporting of Poliomyelitis in Woodbury County, Iowa, and Dakota County, Nebraska*

Week Ending	Sioux City	Rest of Woodbury Co.	Total, Woodbury Co.	Total, Dakota Co.	Total, Both Counties
5/31/52	1	0	1	0	1
6/ 7/52	0	0	0	0	0
6/14/52	1	2	3	0	3
6/21/52	8	4	12	0	12
6/28/52	7	2	9	1	10
7/ 5/52	24	4	28	4	32
7/12/52	25	7	32	2	34
7/19/52*	19	1	20	2	22
Total	86	20	106	9	115

* Data for this week are incomplete because data were collected through July 17 only.

The weekly morbidity of poliomyelitis in these areas in 1952 up until July 17, by date of reporting, is given in table 6. It will be noted that the outbreak began in June and appeared to be increasing steadily. The average delay in reporting, calculated on 97 cases with known date of onset, was 3.7 days. Thus, the picture presented by date of reporting, although not accurate, should be approximately correct. Incomplete data for the last week did not permit the drawing of any conclusions about whether the peak had been passed. There was a total of 115 cases by the time the survey was made. This was a rate of almost exactly 100 per 100,000 for the total population, nearly four times that of the Texas outbreak. Of 104 cases classified by type, only 22% were nonparalytic, and in 29% there was bulbar involvement. The fatality rate for all cases stood at 9.6%. Reporting was believed to be complete in the urban areas at least.

TABLE 7.—*Age Distribution of Patients with Poliomyelitis Reported in Woodbury County, Iowa, and Dakota County, Nebraska, Through July 17, 1952*

Age, Yr.	Sioux City	Rest of Woodbury Co.	Total, Woodbury Co.	Total, Dakota Co.	Total, Both Counties	
<1	3	0	3	0	3	
1	6	2	8	1	9	
2	6	0	6	1	7	
3	5	1	6	0	6	
4	4	1	5	0	5	
5	7	2	9	1	10	70 =
6	5	0	5	0	5	
7	1	1	2	0	2	60.8%
8	3	1	4	0	4	
9	8	1	9	0	9	
10	4	1	5	0	5	
11	1	4	5	3	8	
12	2	0	2	0	2	
13	4	1	5	2	7	
14	4	2	6	0	6	
15-19	3	1	4	0	4	
20-29	12	1	13	0	13	
30 and over	8	1	9	1	10	
Total	86	20	106	9	115	

An examination of the age distribution (table 7) indicated a fairly even distribution in children aged 1 through 11 years, with 60.8% of all cases in this group. In the previous 10 years, 55.7% had occurred in the same age group. The age specific rates in the 1 through 11 year group (table 8) were 310 per 100,000 in Woodbury County and 236 in Dakota County, making an overall rate of 301 in this age group, compared to 93 in Texas. The rate for all other ages, excluding 1 through 11, was 49, compared to 16 in Texas. In five of the six years immediately preceding 1952, rates of 23.6 to 44.5 (1947 rate, 15.8) had been attained in the area as a whole. In Woodbury County, rates for all the previous six years were in excess of 20 per 100,000. Thus, this was the seventh successive "epidemic" year. No large epidemic, such as that of the current year, would have been expected in view of the probable immunity of the population.

Prediction of the probable duration and total morbidity was made after consideration of the distribution by months in the previous decade (table 9). August and September had accounted for the largest number of

cases, with September leading slightly. These were the months of the annual peak incidence. It was, therefore, considered possible that the peak had not been reached by July 21 and that elevated rates would continue for at least two months.

The population in the 1 through 11 year age group (table 8) was estimated at 20,674 for Woodbury County and 2,549 for Dakota County, a total of 23,223. Early appraisal of the community led us to believe that the response would closely parallel that in Utah County, Utah, so it was decided to aim to include in the study 70 to 75% of all children of that age, about 16,500. The area close to the clinics would probably have to respond in an even higher proportion to compensate for a poorer response from the distant, rural areas. It was decided to operate five clinics for at least six days and longer if necessary. Clinical observation of a large sample of cases gave adequate assurance that the disease prevalent was poliomyelitis, a severe type leading to extensive paralysis in a high proportion of cases.

Preparations.—Approvals were readily obtained from state medical societies and health departments as well as from the local health departments and other civil authorities. Officers and selected members of the Woodbury County Medical Society and a five county society in Nebraska, which included Dakota County, encouraged us strongly to believe the total memberships would approve. On the evening of July 16, at a special meeting of the Woodbury County Medical Society, favorable action was unanimously adopted. The society went on record in favor of its members' giving no gamma globulin for poliomyelitis prophylaxis except in our organized clinics. Pharmacists in the community, under the leadership of one member of the profession, also voluntarily agreed to sell no gamma globulin for use in poliomyelitis. A press and radio conference was held on Thursday, July 17, the day after the meeting with the medical society. A novel method of contacting the rural population was specially arranged through the efforts of one of the local women. By means of four rural party-line hookups, two of the chief investigators spoke to what was estimated to be 3,000 people, briefly explaining the project and outlining where and how the listeners could participate. The Houston plan for interesting the community leaders of women's organizations was employed. The response was as good or better. Profiting from experience with large crowds in Houston, the number of women volunteers recruited for each clinic for each four hour shift was increased to 20. Later, 4 to 6 male Army Air Force volunteers served in each clinic during each shift, and a total of 30 local registered nurses came out of retirement to assist our team of nurses in the injection rooms. A variety of suitable sites was selected for the operation of five daily clinics, with scheduled moves for some at one or two day intervals.

TABLE 8.—*Selected Age Specific Incidence and Rate per 100,000 Population of Poliomyelitis in Woodbury County, Iowa, and Dakota County, Nebraska, Reported Through July 17, 1952*

	Woodbury County			Dakota County			Total		
Age, Yr.	Estimated Population	Cases	Rate	Estimated Population	Cases	Rate	Estimated Population	Cases	Rate
1-11	20,674	64	310	2,549	6	236	23,223	70	301
Other ages	83,243	42	50	7,965	3	38	91,208	45	49
Total	103,917	106	102	10,514	9	86	114,431	115	100

TABLE 9.—*Monthly Poliomyelitis Incidence in Woodbury County, Iowa, and Dakota County, Nebraska, 1942-1951*

Month	Sioux City	Rest of Woodbury Co.	Total, Woodbury Co.	Total, Dakota Co.	Total, Both Counties
January	2	1	3	2	5
February	1	0	1	0	1
March	3	1	4	0	4
April	3	1	4	0	4
May	4	3	7	0	7
June	2	1	3	1	4
July	16	6	22	6	28
August	47	14	61	4	65
September	52	16	68	0	68
October	30	7	37	0	37
November	10	6	16	2	18
December	0	1	1	1	2
Total	170	57	227	16	243

Operation of Clinics.—Public attendance at the clinics was in keeping with the cooperation shown by the persons contacted during the planning stages. It appeared as though everyone wanted to attend the clinics on the first day. In the most heavily attended clinics, three to five additional physicians and an equal number of local nurses participated. Additional women and men volunteers were recruited (up to 30 in each clinic) through the efficient volunteer program. One clinic injected 1,447 children in one 8 hour day, equal to that that all five clinics had done in Provo in a 12 hour day. Attendance was so heavy during the first two days that almost half the biologicals were used, but attendance dropped off sharply the last day, giving the impression that almost all those who intended to come had already done so. The daily totals of all clinics were as follows: 4,317; 4,037; 3,812; 2,130; 1,209; and 363, for a total of 15,868 or 68% of the population in the age group from 1 through 11 years.

Results.—Use of gamma globulin from commercial sources never became a problem; its use by any physician in the area must have been rare. No medical complications or reactions were observed in the clinics or reported later by physicians, with the exception of occasional syncope, principally in boys aged 9 to 11, which occured after the patient got up from the injection table. This was probably of psychogenic origin. Fever was occasionally reported, as in the other areas, but again was not attribu-

ted to the injections by the attending physicians. The follow-up team was composed of one epidemiologist-director, two clinicians, one physical therapist, and one secretary.

The peak of the epidemic had actually passed when the selection of the area was made, but the incidence rate continued at a high level. Through August 3, the epidemic for Woodbury County had attained the astounding rate of 402 per 100,000 and for the total area, including Dakota County, 398. Present data, by dates of onset, indicate that the week ending July 19 was the peak week.

Table 10, based on current information as of September 7, with the diagnosis of some cases not completely confirmed or not finally classified by type, shows the weekly incidence of paralytic and nonparalytic cases in the age group of the study (1 through 11 years). It will be noted that 40 paralytic cases occurred in one week (July 27 to August 2), during a period when the injected gamma globulin should have been at maximal titer in the blood. A total of 104 cases (rate of 448 per 100,000) have now occurred in a six week period since the opening

TABLE 10.—*Cases of Poliomyelitis in Woodbury County, Iowa, and Dakota County, Nebraska, in the Age Group 1-11 Years, from July 21 to September 6, 1952, According to Week of Onset*

Week Ending	Paralytic	Nonparalytic	Total
7/26/52	21	2	23
8/ 2/52	40	0	40
8/ 9/52	15	1	16
8/16/52	6	0	6
8/23/52	7	2	9
8/30/52	1	0	1
9/ 6/52	2	7	9
Total	92	12	104

of the clinics. Ninety-two of these (88.5%) were paralytic. In 39 (37.5%) there was bulbar involvement, and 31 of the 39 were bulbospinal in type. The highest age specific rate, 627, occurred in the 2-year-old children. Fifty-eight of the 104 cases occurred in children who attended the clinics.

There is reason to believe that reporting of cases among the children not injected in the clinics is much better than in Texas. It also appears that, proportionally, most of the cases have been occurring in the urban area where the highest proportion of children received injections. Obviously, the only valid analysis will be that based on the comparison of the number of cases in gelatin and gamma gloublin groups of clinic attendants. The investigators have rigidly held to their plans not to seek access to the lists of serial numbers that identify the syringe contents until final diagnoses have been made.

CONSIDERATION OF TESTS IN OTHER AREAS

On closing the Sioux City clinics, the staff was very tired from the long hours and tension of the two consecutive tests. Clinic teams and public relations and administrative personnel were sent home for a rest until August 8, at which time they were to be notified of the decision about a subsequent test. On August 7, a careful count was made of all probable cases occurring in the clinic injected groups in the Texas and the Iowa-Nebraska areas (59 cases), and the trends of both outbreaks were carefully studied. Enough biologicals remained for one relatively small test. The investigators agreed that the number of cases that would be expected to occur in the 54,772 children injected in the Utah, Texas, and Iowa-Nebraska projects should readily furnish the answer to the principal question of whether the Red Cross gamma globulin in the dose used would give significant protection and that, if it does, there would probably also be some rough indication of the duration of that protection as well. Any subsequent, small study conducted in late August would not contribute significantly to the question regarding the duration of protection, because of the shortness of the remaining epidemic season. Adequate laboratory specimens for studies regarding possible interference with inapparent infection and the development of active immunity would be obtained from the current studies plus that of Utah. Therefore, a decision was reached that no further field tests need be undertaken.

PLANS FOR REPORTING RESULTS

A tabulation of all cases with completed 30 day follow-up examinations appears in this issue (page 757). A final clinical diagnosis and classification of paralytic or nonparalytic type of involvement will have been made for each of these. Then one person not engaged in the study, by consulting the key list of serial numbers, will determine what type of inoculum each patient had received. An analysis of these findings will be prepared by the investigators and will be reported at the earliest possible date. A final report of all cases together with an evaluation based on the degree of paralytic involvement as determined by the 60 day examination will be presented subsequently.

SUMMARY

As a result of the experience gained in the 1951 pilot test of the use of gamma globulin in the prophylaxis of poliomyelitis in Utah, certain minor modifications of plans were made for the definitive tests of 1952, but in all essential elements the tests were similar, so the results of all could be combined for analysis. In July, 1952, 33,137 children, aged 1 through 6 years, in Harris County, Texas, and 15,686 children aged 2 through 11 years in Woodbury County, Iowa, and Dakota County, Nebraska received injections of either Red Cross gamma globulin or gelatin. Cooperation and participation by the medical profession and the public were of an extremely encouraging nature, as they were in the pilot study. The epidemics selected have continued in such a manner that 85 cases have occurred already in the inoculated group and cases continue to occur. Since it is not yet known which of the two materials (gamma globulin or gelatin) had been injected in any child who subsequently had poliomyelitis during the course of the epidemics, no conclusions can be drawn regarding the results, except that the number of cases will be large enough to give a highly significant answer. A preliminary report of results will be presented in the near future, when final clinical diagnoses have been established for a majority of the cases.

EVALUATION OF RED CROSS GAMMA GLOBULIN AS A PROPHYLACTIC AGENT FOR POLIOMYELITIS

3. PRELIMINARY REPORT OF RESULTS BASED ON CLINICAL DIAGNOSES

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The plan and accomplishment of a series of three controlled field trials to evaluate the effectiveness of Red Cross gamma globulin in the prevention of poliomyelitis were described in the previous two papers (see this issue, pages 739 and 750). Effectiveness was to be determined by comparing the number of paralytic cases occurring in two groups receiving injections, one inoculated with gamma globulin, the other with gelatin. The groups were comparable, being essentially of equal size and presumably similar in all other respects, owing to the method of random distribution employed in packaging the two types of biologicals. Both biologicals were similarly labeled and looked alike. The serial number borne by each unit was the only means of identification. This serial number, obtained from the container of material inoculated, was entered on the record of each child. The key to the contents of all units was maintained in a central agency in New York. Thus, knowledge as to the inoculum received by any one child was not available to anyone, including the investigators, until the final diagnosis was established.

A total of 54,772 children had been inoculated in September, 1951, in Utah, and in July, 1952, in Texas, Iowa, and Nebraska during epidemics of poliomyelitis. Every effort was made to obtain complete reporting of all cases of definite or suspected poliomyelitis in the age group of the study, in both children receiving injections and those not receiving injections. All patients so reported on were examined repeatedly by clinicians and physical therapists of the follow-up teams. Conferences were held at frequent intervals with the field teams by one or more of the principal investigators. All records were examined critically in order to arrive at the most accurate clinical diagnosis and to determine whether those patients accepted as having poliomyelitis had the paralytic or the nonparalytic type of the disease. A patient was classified in the paralytic group if found to have definite muscle weakness that could not be attributed to tenderness, "spasm," general debility, normal asymmetry, anomaly, or any cause other than poliomyelitis. Examinations made from 10 to 30 days after onset were considered of greatest importance in detecting significant, minor involvement. In some patients complete recovery had occurred by the time the 60 day examination was made, but such a patient was still considered to have been in the paralytic group. In our tentative system of classification these were listed as grade 1. The other gradings are described in table 3.

On Oct. 1, 1952, a list was made of the 90 patients in the three study groups of inoculated children who had contracted paralytic poliomyelitis at some time after the date of injection and who had been followed for at least 30 days. The serial number of the inoculum that each paralytic patient had received was listed. Information as to the nature of the inoculum, whether gamma globulin or gelatin, was obtained from the central agency in New York. A preliminary analysis of these 90 cases is the subject of this report, which is purely tentative and covers only limited aspects of the problem. A complete analysis of the data based on clinical observations will be made after the termination of the current outbreaks and the end of the follow-up period. A final report will be made after completion of all laboratory aspects of the study.

The number of cases of paralytic poliomyelitis occurring among the children who received injections in each of the three study areas, by type of inoculum and by the time of onset after inoculation, is shown in table 1. Those occurring within seven days after injection are listed by single days, and those occurring subsequently by weekly intervals. This tabulation includes only a portion of the cases occurring during the eighth week in Iowa-Nebraska and the ninth week in Texas and none subsequent to these times, since follow-up studies on most of the later cases have not been completed. The last case occurring in Utah in 1951 was during the 12th week. The percentage of cases of paralytic disease that occurred among those receiving gamma globulin, by time intervals, is given in table 1 and is presented graphically in figure 1. The onset and approximate duration of protection by gamma globulin against clinically recognizable paralytic poliomyelitis may be observed in this graph and table.

The cumulative total of patients with paralytic poliomyelitis in each group is given in table 2 and is shown graphically in figure 2. The graph illustrates particularly the time when protection first became apparent and the total number of children who appear to have been protected. A cumulative percentage column for the gamma globulin group is included in table 2. This shows the

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period of decreasing and increasing percentage of cases in the children who received injections of gamma globulin.

As shown in table 1, there were 64 patients in the group receiving gelatin and 26 in the comparable gamma globulin group out of a total of 90 patients observed. These crude differences are statistically significant. It will be noted that during the first week there does not appear to have been any significant degree of protection, 12 cases occurring among those receiving gamma globulin and 16 among those receiving gelatin. Even on the seventh day the four cases were equally divided. During the second week, however, there was a marked difference between the number of cases in the gamma globulin and gelatin groups, in which there were 3 and 23 cases respectively. The reduction appears to have been greatest during this week, but protection appears to have continued through the fifth week. From the second through the fifth week only 6 cases occurred among those receiving gamma globulin and 38 among those receiving gelatin. This difference is highly significant. Because of the waning epidemic trends and the present incompleteness of the follow-up study in the Iowa-Nebraska area, in particular, there are not enough cases in any one week, or even by grouping several weeks, to determine exactly the duration of protection. Analysis of subsequent data should give more precise and reliable information regarding the duration of protection.

Since it was planned to make all comparisons of severity on the basis of the 60 day muscle examination (see this issue page 746), no complete analysis of this has been attempted. However, 60 day severity gradings have been made on the group of cases occurring during the first week after injection, that period of time during which the number of cases was not significantly decreased by the injection of gamma globulin. Tables 3 and 4 present the analysis of severity and extent of paralysis. In table 3, numbers of patients in the two groups who received inoculation are tabulated by the degree of maximal severity noted in any muscle without regard to the number of muscles involved. The comparison between the two groups who received injection suggests that the disease was modified, though not prevented, in children with onset of illness seven days or less after receiving gamma globulin. In table 4 the same cases are tabulated by the extent rather than by the severity of paralysis. The number of areas involved, one through seven, represents muscle involvement in any of the four extremities, the neck, the trunk (back, abdomen, intercostal group, etc.), or the muscles innervated by bulbar centers (palate, pharynx, face, etc.). When no area is shown as involved, as in 6 of the 12 patients receiving gamma globulin, complete recovery had occurred during the 60 day period of observation. None had recovered completely in the other group. Here again, it will be noted that the disease was probably modified when gamma globulin was given during the last week of the incubation period. It should be emphasized that the examiners who rated the extent and degree of muscle involvement did not know whether the child being examined had received gamma globulin or gelatin.

TABLE 1.—*Number of Cases of Paralytic Poliomyelitis Among Inoculated Children in Three Study Areas, by Place, by Type of Inoculum, and by Time After Injection*

Interval After Inoculation		Utah		Texas		Iowa-Nebraska		Total			
Days	Weeks	Gamma Globulin	Gelatin	Gamma Globulin	Gelatin	Gamma Globulin	Gelatin	Gamma Globulin	Gelatin	Total	Gamma Globulin, %
1	..	0	0	1	1	1	1	2	2	4	—
2	..	0	0	1	0	0	0	1	0	1	—
3	..	0	0	1	0	0	2	1	2	3	—
4	..	0	0	1	0	1	3	2	3	5	—
5	..	0	0	0	0	3	2	3	2	5	—
6	..	0	1	0	1	1	3	1	5	6	—
7	..	0	0	0	1	2	1	2	2	4	—
Total	1	0	1	4	3	8	12	12	16	28	42.9
..	2	0	1	1	7	2	15	3	23	26	11.5
..	3	0	0	1	4	1	4	2	8	10	20.0
..	4	0	0	1	2	0	2	1	4	5	12.5
..	5	0	0	0	1	0	2	0	3	3	
..	6	1	1	2	0	0	3	3	4	7	42.9
..	7	0	0	1	1	2	3	3	4	7	
..	8	0	0	0	0	1	0	1	0	1	
..	9	0	1	1	0	—	—	1	1	2	50.0
	10+	0	1	—	—	—	—	0	1	1	
Total	2-10+	1	4	7	15	6	29	14	48	62	22.6
Total	1-10+	1	5	11	18	14	41	26	64	90	28.9

TABLE 2.—*Cumulative Number of Cases of Paralytic Poliomyelitis in Children from All Three Study Areas, by Type of Inoculum and by Week After Injection*

Weeks After Inoculation	Gamma Globulin	Gelatin	Total	Percentage in Patients Receiving Gamma Globulin
1	12	16	28	42.9
1-2	15	39	54	27.8
1-3	17	47	64	26.6
1-4	18	51	69	26.1
1-5	18	54	72	25.0
1-6	21	58	79	26.6
1-7	24	62	86	27.9
1-8	25	62	87	28.8
1-9	26	63	89	29.2
1-10+	26	64	90	28.9

COMMENT

Conclusive evidence of a very significant reduction in the total number of cases of paralytic poliomyelitis occurring during three epidemics as a result of injecting Red Cross gamma globulin is presented. This reduction was effected by injecting a dose averaging 0.14 cc. per pound of body weight. The disease does not appear to have been prevented when the injection was made during the last seven days of the incubation period; how-

ever, modification probably occurred, since all patients with onset during the first week had mild disease and half had recovered completely in 60 days. The total duration of prevention and possible modification of disease during the waning period of protection have not been established by these preliminary data. However, it appears that, after the first week following inoculation, marked protection was afforded that lasted through the fifth week, at least. Although no data are available yet, it would appear possible that modification of the disease might occur during the period of waning or incomplete protection.

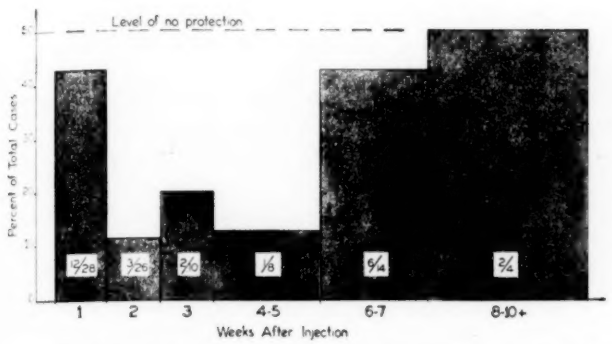

Fig. 1.—Percentage of cases of paralytic poliomyelitis in the study groups that occurred in children who had received gamma globulin, by intervals after injection.

Several points might be emphasized in respect to the general validity of these results. Studies were performed in two different years and in three widely separated geographical areas. One of these, Harris County, Texas, included Houston, a very large metropolitan area, where many strains of virus might well have been present. Results of all three tests were similar; that is, fewer cases occurred in the children who received gamma globulin. Under these circumstances it is highly probable that the results obtained were not those of a test against a single immunologic type of poliomyelitis virus. Thus, it appears probable that Red Cross gamma globulin as used in these studies will prevent poliomyelitis in other epidemic areas. The great severity of the disease in the Sioux City area, as judged by the high proportion of bulbar cases, the extent of paralytic involvement, the high case fatality rate, and the phenomenal morbidity rate (greater than 400 per 100,000) in the wake of six consecutive previous epidemic years (see this issue, page 750) testifies to the great invasiveness or virulence of the strain or strains active in that area. Even under these circumstances highly significant protection was demonstrated. These findings afford strong evidence that Red Cross gamma globulin or any other product shown to have an equal or greater antibody titer to the three recognized immunologic types of virus will confer significant protection against paralytic poliomyelitis when given in the dosage employed in these tests. This protection should be manifest through both modification and prevention of the disease. The duration of protection can undoubtedly be extended significantly beyond the five to seven week period by increasing the size of the original dose or by repeating the injection. As pointed out in an earlier paper (see this issue, page 750) evidence based on half-life studies of homologous gamma globulin indicate that doubling the dose will extend the protection approximately three weeks in children of the most susceptible age group and about two weeks in adults.

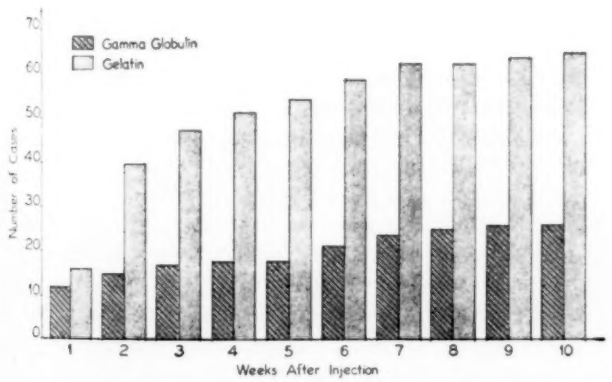

Fig. 2.—Cumulative number of cases of paralytic poliomyelitis among children inoculated with gamma globulin or with gelatin, by weeks after injection.

TABLE 3.—*Severity of Paralysis Occurring Within Seven Days of Inoculation of Children with Gamma Globulin or Gelatin*

Severity of Paralysis *	No. of Patients: Gamma Globulin	No. of Patients: Gelatin
Grade 1	6	0
Grade 2A	6	11
Grade 2B	0	2
Grade 3	0	3
Total	12	16

* Based on findings of examination made 60 days after onset on patients showing definite weakness during earlier examinations. Grade 1 represents normal muscle power, i. e., complete recovery in a formerly paralyzed patient. Grade 2A represents normal to good muscle power and grade 2B good to normal but some fair muscle power. Grade 3 represents trace, poor or fair muscle power, i. e., the severest residual involvement.

TABLE 4.—*Extent of Paralysis Occurring Within Seven Days of Inoculation of Children with Gamma Globulin or Gelatin*

No. of Areas Involved *	No. of Patients: Gamma Globulin	No. of Patients: Gelatin
0	6	0
1	1	5
2	1	3
3	2	5
4	2	1
5	0	2
6	0	2
7	0	0
Total	12	16

* Based on findings of examination made 60 days after onset in patients showing definite weakness during earlier examinations. The seven areas include four extremities, neck, trunk, and muscles innervated by bulbar centers.

The practical range of usefulness of this agent cannot be defined at present. If, however, after completing the laboratory aspects of this study, it is found that gamma globulin has not interfered with inapparent infection and the development of active immunity during the period of protection against clinical disease, this agent will have a wide field of usefulness, at least until a more effective and equally safe means of prevention has been developed. All animal studies to date support the belief that gamma

globulin will not interfere with the development of active immunity. Even if or when a more effective and/or permanent means of prophylaxis becomes available, immediate passive protection will still have a place in the armamentarium of the general practitioner, internist, pediatrician, and health officer. It may also prove to be useful in conjunction with a viral vaccine.

SUMMARY

In a series of three controlled field tests to evaluate the prophylactic effect of Red Cross gamma globulin in poliomyelitis, 54,772 children between the ages of 1 and 11 years were inoculated, one-half of them with gamma globulin and one-half with a solution of gelatin. These three field tests were conducted in areas that were experiencing severe epidemics of poliomyelitis. The injections were given to apparently normal, healthy children living in the area, with the full understanding, permission, and cooperation of the parents. Which of the two materials any one child had received was unknown to all—children, parents, and investigators—until completion of a follow-up period considered to be adequate for determining a final diagnosis.

A preliminary tabulation of results as of Oct. 1, 1952, shows that paralytic poliomyelitis had been diagnosed in 90 cases in the study groups. Analysis of these patients on the basis of the type of injection received shows that significant protection was conferred by the gamma globulin. During the first week after injection there was no significant reduction in the number of cases in the group receiving gamma globulin, but the severity of paralysis appears to have been modified. From the second through the fifth weeks highly significant protection was demonstrated. After the fifth week this was less evident, but more definite conclusions regarding the duration of protection and possible modification of disease should be available after a longer period of follow-up. Laboratory studies, still incomplete, should give information regarding the effect of gamma globulin on inapparent infection and the subsequent development of active immunity.

TREATMENT OF HICCUPS

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Benign, self-limited hiccups are common phenomena experienced by almost everyone at some time or another. However, persistent hiccups may cause the victim great distress and be refractory to most treatments. Patients are first distressed, later endangered by persistent hiccups. Vomiting, acid-base and fluid imbalance, malnourishment, and exhaustion may follow. In the postoperative patient, wound dehiscence is an added danger. Methods of treatment from the simplest to the severest must be tried successively until relief is obtained. Because hiccups may be such a dangerous complication during and after surgery, this paper will review the experiences of others in addition to some of our own in the hope of achieving the best possible management of the problem.

A hiccup is described by Smith [1] as a pathological respiratory reflex characterized by a clonic spasm of the diaphragm, which results in a sudden inspiration. This, in turn, is abruptly terminated by closure of the glottis, which is audible to a variable degree. Hiccups are usually superimposed on a normal respiratory cycle. Actually, the mechanism is not always this simple. Campbell [2] described a 76-year-old man in whom hiccups were still present following bilateral phrenicectomy. Thus, it is evident that not only the diaphragm but also all other muscles of respiration may become involved in the clonic spasms of hiccups. A modified type of hiccup may be observed during endotracheal anesthesia. In such cases, sudden closure of the glottis is obviously not a component part of the reflex.

The neural mechanisms involved in hiccups are complex. When the cause is not central, the afferent pathways may be many and varied. It is thought by Bailey [3] and other observers that stimulation of the vagus and the phrenic nerve endings is a common etiological factor. This appears reasonable, since peripheral stimulation is so often the result of irritation of the stomach, intestine, peritoneum, pleura, or diaphragm. Other peripheral pathways have been incriminated. Byrnes [4] described a case of tabes dorsalis in which irritation of the lower dorsal segments of the spinal cord was thought to be the cause, since such stimulation paralleled the sensory innervation of the periphery of the diaphragm. Hiccups have been initiated during operations on the prostate gland and on the extremities, postulating other varied afferent pathways. The vagus nerve (to larynx and lung), the phrenic nerve (to the diaphragm) and the upper spinal nerves (to the intercostal muscles) are apparently the principal efferent limbs that act in response to the respiratory centers in the brain.

ETIOLOGY

The etiology of hiccups, which is probably the most important consideration in directing satisfactory treatment, is complex. Several classifications have been outlined in the literature, but probably a simple grouping into peripheral and central causes is the most useful. Common peripheral causes are irritation or dilatation of the stomach, intestine or peritoneum, subphrenic abscess, perihepatitis, and diaphragmatic and other hernias. Pul-

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Because of lack of space, some of the bibliographic references have been omitted and will appear in the authors' reprints.

Read before the Section on Anesthesiology at the 101st Annual Session of the American Medical Association, Chicago, June 11, 1952.

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monary diseases such as tumors, pleurisy, laryngitis, bronchitis, or pneumonia may be factors at times. Mediastinal [1] and esophageal lesions, cardiac enlargement, and pericarditis have been implicated. In order of their incidence, Bailey [3] found hiccups to be greatest in bladder and prostatic operations, followed next by colon operations (particularly if obstruction was present) and then by peritonitis. Weiss [5] encountered three cases of severe hiccups that complicated acute coronary occlusion. Another persistent case of hiccups was described as the sole symptom of a large aneurysm of the thoracic aorta.[6]

Hiccups that occur as a result of central causes are probably commoner than is often realized. Benign hiccups are frequently produced by tobacco, alcohol, or mental reactions.[7] Uremia is a classic cause of hiccups. They have been observed in many toxic conditions such as gout, malaria, and influenza. Further etiological factors of central origin as reported by Smith [1] are encephalitis, brain tumors, hydrocephalus, and meningitis. Robinson, Robinson, and Feaster [8] reported hiccups that occurred during insulin shock therapy. This finding was believed to be an empirical sign of impending complications. Fetal hiccups observed in 21 cases by McGee [9] were shown to be allergic manifestations on the part of the mother and the baby.

TREATMENT

Treatment is notably disappointing, as is evidenced by the hundreds of remedies that have been tried, none of which have been regularly curative. Simple hiccups, which are self-limited, may respond to many different treatments and pharmacologically dissimilar drugs. These benign types, often the result of simple gastric irritation, may respond well to carminatives. Other remedies include physical or psychic counterirritative methods such as traction on the tongue, inhalation of ether fumes, drinking cold water, and sudden fright. Sedatives, such as bromides and the barbiturates, often give relief.

However, the solution of the problem of treating persistent hiccups requires more than empirical remedies. The cause should be corrected, whenever one is suspected. Since dilatation and irritation of the stomach are such common etiological conditions, gastric lavage is often the first therapeutic step. Antispasmodic drugs, for example, amyl nitrite, may be helpful. Nairn [10] reported one case of hiccups that lasted four days and was cured by amyl nitrite inhalations after many other remedies had failed. Shaine [11] has shown that benzedrine sulfate has a specific gastrointestinal antispasmodic effect and has reported a favorable response to this drug in two patients who had hiccups. Central etiological factors should not be overlooked since many such conditions may be treated effectively. In this respect, the urinary output and nonprotein nitrogen should be measured if uremia is suspected.

Even though the cause remains unknown, several drugs and procedures may be used as a rational treatment for intractable hiccups. Other more empirical measures are frequently helpful. It is important to follow a definite sequence of therapeutic steps until the condition is relieved.

Counterirritation.—It is surprising how many patients with hiccups respond to digital compression of the eyeballs. This pressure through the closed lids is exerted to the point of mild discomfort and maintained for several minutes. As is the case with many other empirical treatments, such as pressure on the upper lip to stop sneezing, the reason for the frequent success of this method is not entirely clear. Vomiting, initiated by pharyngeal irritation or apomorphine, is frequently effective in stopping hiccups.

Gastric lavage.—If counterirritation fails, the stomach should be washed out to remove any irritant.

Atropine.—This drug is very effective in relieving hiccups. As an antiparasympathetic agent, it acts by blocking the vagal limb of the reflex arc. It is effective when given intravenously in relatively high doses, 1/150 to 1/50 grain (0.4 mg. to 1.2 mg.).

Heavy Sedation.—Depression of the central nervous system can be achieved by administration of opiates or barbiturates. Many cases of hiccups are alleviated by this method.

Carbon Dioxide.—Carbon dioxide is a very powerful stimulant to the respiratory center in the brain. High concentrations of carbon dioxide in lung air and blood produce a considerable increase in the depth of respiration. Inhalation of carbon dioxide is extremely effective in stopping hiccups. This forms the basis of several popular lay remedies, such as breathing in and out of a paper bag and breath-holding.

A simple method of raising the carbon dioxide blood level makes use of two or three conduits from an anesthesia machine linked together. The patient breathes in and out of one end of the tubing. This apparatus serves as a substantial prolongation of the patient's anatomical dead space. This dead space is the purely conductive part of the respiratory tract down to but excluding the pulmonary epithelium through which gases are interchanged between lung air and blood. On expiration, much of the exhaled gases, including carbon dioxide, remains in the joined conduits and is rebreathed during the next inspiration. The carbon dioxide, thus rebreathed, is added to the normal tension of this gas in the lungs, and the blood level in the lungs soon rises. The capacity of the rubber conduits must be less than the tidal volume or the patient will soon use up most of the oxygen originally inhaled, be deprived of further oxygen, and become anoxic (fig. 1).

Phrenic Nerve Block.—When all of the above treatments fail, more vigorous and radical measures must be instituted. This can be accomplished by blocking or crushing one or both phrenic nerves, and so interrupting the efferent limb of the reflex arc. The phrenic nerve may be blocked by the supraclavicular approach, or by

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11. Shaine, M. S.: Benzedrine Sulphate in Persistent Hiccough: Report of 2 Cases, Am. J. M. Sc. **196**: 715-717 (Nov.) 1938.

the posterior paravertebral injection of the third, fourth, and fifth cervical roots. Diaphragmatic paralysis on the side so treated may be demonstrated by fluoroscopic examination of the chest. If one block is not effective, the second side may be blocked after the function of the first has been regained. This procedure frequently affords permanent relief and may be repeated several times if hiccups recur. However, if permanent relief is not obtained by this method of nerve interruption, it will be necessary to crush one or both phrenic nerves. The blocking of nerves beforehand permits an evaluation of the pulmonary function and the degree of respiratory embarrassment subsequent to diaphragmatic paralysis. If a unilateral block is ineffective in stopping the hiccups, both sides may then be done at the same time. In

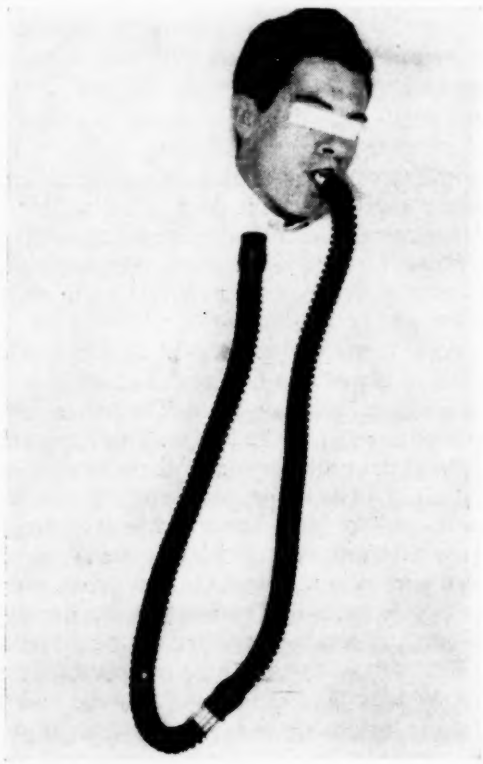

Fig. 1.—Apparatus for producing hyperventilation by rebreathing through linked conduits from an anesthesia machine.

such instances, certain precautions, which are described in the next section dealing with phrenic crush, must be taken. This sequence of blocking one or both phrenic nerves, then, if necessary, crushing one or both nerves, permits a study of the pulmonary function to be made while diaphragmatic inactivity is only transient, before instituting prolonged paralysis of the diaphragm.

Phrenic nerve crush.—At this clinic, phrenic nerve section and phrenic nerve crush have been used in the treatment of obstinate hiccups. Unilateral and bilateral operations have been performed. Although both sides were done at the same time in one patient, in all others in whom bilateral operations were performed the two procedures were spaced days or weeks apart. In recent years, phrenicectomy has been abandoned in favor of the crush operation. It is believed that the permanent paralysis that results from nerve section is unwarranted when the duration of the effect of a phrenic crush is almost always sufficient for permanent relief of the hiccups. Not only this, but the desired result is usually obtained following the crush of only one phrenic nerve.

It appears wiser to crush the left nerve rather than the right for the following reasons [12]:

1. Clonic contractions of the left diaphragm distress the patient more than those on the right, since the left diaphragm slaps and tugs on the heart and stomach with each hiccup and jerks on the esophagus as it enters the abdomen and the liver has a moderate splinting action on excessive movement of the right diaphragm. 2. Clinical experience indicates that crushing of the left phrenic nerve will relieve most intractable hiccups.

Occasionally, unilateral diaphragmatic paralysis fails to stop the trouble. After careful consideration the other phrenic nerve may be crushed, but this is never done under the following conditions: during the same 24 hour period as the first nerve crush; in the presence of severe cardiorespiratory disease, such as emphysema, when there is marked reduction of vital capacity or exercise tolerance; if the patient displayed dyspnea or cyanosis during or following the first phrenic crush; without careful evaluation of cardiac and pulmonary function after the previous crushing; and without facilities in the operating room for resuscitation and oxygen therapy. Preparations should be made for tracheal intubation and artificial respiration with an anesthesia machine. A Drinker or Emerson type respirator should also be available in case of prolonged respiratory arrest. The following cases illustrate the refractoriness of persistent hiccups to treatment, and the extensive therapy that must be utilized in order to obtain relief.

REPORT OF CASES

CASE 1.—The first patient was a man in whom hiccups developed 28 days following a subtotal gastrectomy for peptic ulcer. Atropine, 1/150 grain (0.4 mg.), was injected intravenously, but there was no improvement. Carbon dioxide inhalations were tried. These also were ineffective. A right, paravertebral, procaine block of the third, fourth, and fifth cervical nerve roots resulted in hemiparesis of the diaphragm, and the hiccups stopped completely. Unfortunately, they recurred in four to five hours and persisted intermittently. The following day the phrenic block was repeated with the same good result as before. Again the trouble returned as the procaine effect wore off. Using the supraclavicular approach, a length of plastic tubing was inserted down to the right phrenic nerve through a large-bore intravenous needle. Fractional doses of 2% procaine were given, and the hiccups ceased for several hours, but even this treatment soon became ineffective.

Use of the electrophrenic stimulator, as described by Sarnoff,[13] was then considered. This instrument is designed to induce artificial respiration by stimulation of the phrenic nerve. An electric current, which rises from zero to a peak and then falls again, is transmitted through an electrode placed over the phrenic nerve motor point in the neck and causes rhythmic diaphragmatic contractions. This type of stimulation was given to this patient in the hope of stopping his trouble. It partially established control of this diaphragmatic activity but distressed him considerably and did not cure the hiccups. They remained superimposed on his artificially regulated breathing. Finally, the left phrenic nerve was exposed and crushed, with dramatic relief of the hiccups. When the patient was seen a month later the hiccups had not recurred.

13. Sarnoff, S. J.; Hardenbergh, E., and Whittenberger, J. L.: Electrophrenic Respiration, Am. J. Physiol. **155**: 1-9 (Oct.) 1948.

CASE 2.—The second patient, a man, was admitted for treatment of hiccups of unknown etiology that had existed for several days. The results of conservative approaches were disappointing. A left phrenic nerve block, by the paravertebral method, paralyzed the left diaphragm but had little effect on the hiccups. The following day, a right phrenic nerve block relieved the hiccups for two to three hours. Electrophrenic stimulation was then instituted to control diaphragmatic movement. Although the severity of the hiccups lessened, they did not disappear. A right phrenic nerve crush was carried out a day later without benefit. Twenty-four hours afterward the left nerve was exposed and crushed. The hiccups ceased immediately. Three weeks later they had not returned. Despite the usual plan of crushing the left nerve first, the right phrenic was paralyzed after a fluoroscopic examination indicated greater activity of the right diaphragm. Perhaps a bilateral operation would have been unnecessary if the left side had been done first.

In 20 to 30% of the cases in which the phrenic nerve is crushed, there is an accessory phrenic nerve.[14] It arises from the fifth cervical or the nerve to the subclavius muscle and joins the main nerve in the thorax. This probably accounts for the occasional failure to obtain diaphragmatic paralysis after crushing of the phrenic nerve. For the operation to be effective, the secondary nerve must also be located and crushed (fig. 2).

HICCUPS DURING SURGICAL TREATMENT

As anesthesiologists, we have a special interest in the management of intractable hiccups that occur during anesthesia and operative procedures. This complication has been encountered during all types of surgical procedures, but the large percentage of times it appears during an abdominal operation is striking. This view is also shared by Knight.[15]

In the typical case, the patient is under spinal anesthesia lightly supplemented by one or more general agents. The hiccups begin most often during manipulation of and traction on upper abdominal viscera. Tugging on organs and their peritoneal attachments in the upper portion of the abdomen stimulates the vagus nerve endings that supply them. Palpation and manipulation of the diaphragm involve stimulation of its phrenic nerve fibers. As already seen,[3] the vagi and the phrenic nerves are the two principal factors in the production of hiccups. It is significant that during spinal anesthesia for abdominal operations the only nerves entering the field of operation that have not been anesthetized are the phrenic nerves (originating from the third, fourth, and fifth cervical segments) and the vagus nerves (cranial outflows of the parasympathetic system). Prophylactic and therapeutic measures are notably effective in these patients.

PREVENTIVE MEASURES

For prophylaxis it is logical to obtund reflex activity of these two nerve systems in patients undergoing surgical treatment (or merely exploration) in the subdiaphragmatic region. This is partially achieved by including in the premedication one of the antiparasympathetic drugs, atropine or scopolamine. In the operating room, the spinal analgesia is supplemented by a light plane of general anesthesia. When this supplement is established and properly maintained, it is impressive how seldom hiccups will occur. Of course, this additive narcosis is not carried out solely to prevent hiccups, but is instituted primarily to produce a more comfortable patient and a more tranquil operative field than otherwise would be obtained. The prevention of hiccups is merely one of the accruing benefits.

MANAGEMENT DURING SURGICAL PROCEDURES

When hiccups occur during an operation, several therapeutic approaches are considered. Although many of these measures are admittedly empirical, it is the obligation of the anesthesiologist to work out a definite sequence of treatment, such as that listed below, and institute each step in turn until the hiccups stop.

1. The anesthesia is deepened to raise the threshold of irritability of the afferent limb of the reflex arc. 2. Atropine, 1/150 to 1/50 grain (0.4 mg. to 1.2 mg.), is given intravenously to produce parasympathetic inhibition. 3. Carbon dioxide accumulation is the next step, which is achieved through by-passing the carbon dioxide absorber on the anesthesia machine. This is continued for only a few minutes so as not to disturb, dangerously, the patient's blood chemistry or produce gross hyperventilation that might prevent the surgeon from doing his best work. 4. Mild, positive pressure applied to the rebreathing bag of the anesthesia machine will frequently produce a more normal pattern of respiration. 5. An endotracheal tube is inserted if the above measures are ineffective. This will not stop the hiccups, but by keeping the glottis open it will reduce the force of the hiccups and quiet the surgical field considerably. 6. In very severe cases in which the hiccups preclude continuance of surgical treatment the experienced anesthe-

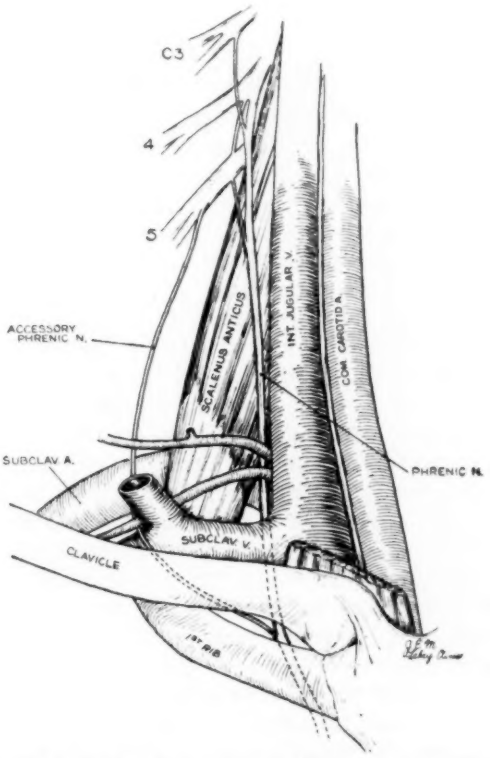

Fig. 2.—Drawing showing the relationship of the accessory phrenic nerve to the main phrenic nerve and other adjacent structures.

14. Bailey, H., and Love, R. J. M.: A Short Practice of Surgery, ed. 4, London, H. K. Lewis & Co., Ltd., 1938.

15. Knight, R. T.: Present Developments in Combined Anesthesia, J. Michigan M. Soc. **46**: 90-91 (Jan.) 1947.

siologist may consider completely paralyzing all muscles of respiration. This serious measure is carried out after tracheal intubation and consists of paralyzing the muscles of respiration with a drug such as *d*-tubocurarine or decamethonium bromide. Artificially controlled respiration with the use of an anesthesia machine is then instituted. The danger of this procedure in inexpert hands or with a poor risk patient cannot be overemphasized.

CONCLUSION

In the management of persistent hiccups, a definite sequence of therapeutic measures should be followed until permanent relief is obtained. These begin with the simplest medical steps and progress to the most radical but most effective treatment, the crushing of the phrenic nerve.

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PROGNOSIS IN IDIOPATHIC HEMOPTYSIS

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and
David T. Carr, M.D., Rochester, Minn

Expectoration of blood may be caused by many disorders. In some instances thorough investigation fails to disclose the cause of this symptom and the patient may be said to have idiopathic hemoptysis.

Several authors [1] have suggested that hemoptysis in the absence of demonstrable causative disease may be due to ulceration of the mucosa of small bronchi. Other possibilities have been suggested: namely, small pulmonary infarctions; vicarious menstruation; blood dyscrasias; and systemic and pulmonary hypertension.

The frequency of idiopathic hemoptysis as reported in the literature varies considerably, depending on the method of selection of cases and the thoroughness of their study. Chaves [2] studied a group of 325 patients who had had hemoptysis less than three months before they were examined in a New York City chest clinic; 189, or 58.1%, of these had no objective evidence of thoracic disease at the time of examination. Jackson and Diamond [1a] reported a series of 436 patients who had hemoptysis in a degree warranting a bronchoscopic examination. No evidence of disease was found in 34 patients (7.8%), and an additional 74 (16.9%) had only generalized tracheobronchitis. In a similar study of 200 patients Moersch [3] found that 11 (5.5%) had no demonstrable disease and 18 (9%) had only chronic bronchitis.

It has been our clinical impression that the prognosis in such cases is good. Heller [4] and Jackson and Diamond [1a] agreed with this opinion, but their studies were not designed to determine the long-range significance of unexplained hemoptysis. In the hope of clarifying this issue we studied a group of patients having idiopathic hemoptysis with particular attention to the prognosis. To accomplish this, we surveyed the records of the Mayo Clinic for the years 1942 through 1946. We selected all the cases of hemoptysis in which no causative disease was found despite thorough investigation. Roentgenographic, bronchoscopic, and bronchographic examinations had been performed in all cases. Pertinent data were summarized from the case records, and follow-up information was obtained from records of recent examinations at the clinic and by correspondence with the patient or his family. Seventy-five cases were available for study.

TABLE 1.—*Age and Sex Incidence of Patients with Idiopathic Hemoptysis*

Age, Yr.	Women	Men	Total
10-19	1	1	2
20-29	3	5	8
30-39	8	12	20
40-49	8	15	23
50-59	6	11	17
60-69	1	4	5
Totals	27	48	75

TABLE 2.—*Duration of Idiopathic Hemoptysis Before Examination*

Patients	Less Than 1 Month	1 to 12 Months	More Than 12 Months	Total
Women	2	15	10	27
Men	16	17	12	45
Total	18	32	22	72*

* Unknown in 3.

The age and sex incidence is given in table 1, the duration of the hemoptysis prior to examination at the clinic in table 2, and the severity of the hemoptysis in these cases in table 3. A majority of the patients were more than 30 years old, and men outnumbered women 2 to 1. The data in table 2 suggest that men are more frightened by hemoptysis than are women, as more of them sought medical advice without delay. Almost all of these patients had gross hemoptysis (table 3), as only a few patients with minimal blood streaking of the sputum were studied thoroughly enough to be included in this investigation.

A follow-up report five or more years after examination was obtained from 55 of these 75 patients. The survival rate, calculated by the method of Berkson and Gage,[5] showed that 50 patients, 90.9%, were still alive.

From the Division of Medicine, Mayo Clinic.

1. (*a*) Jackson, C. L., and Diamond, S.: Haemorrhage from the Trachea, Bronchi and Lungs of Nontuberculous Origin, Am. Rev. Tuberc. **46**: 126-138 (Aug.) 1942. (*b*) Abbott, O. A., and Hopkins, W. A.: The Clinical Significance of Hemoptysis: A Study of 1316 Patients with Chest Disease, J. M. A. Georgia **36**: 360-371 (Sept.) 1947. (*c*) Wessler, H.: Notes on Hemoptysis, J. Mt. Sinai Hosp. **7**: 548-553 (Jan.-Feb.) 1941.

2. Chaves, A. D.: Hemoptysis in Chest Clinic Patients, Am. Rev. Tuberc. **63**: 194-201 (Feb.) 1951.

3. Moersch, H. J.: Clinical Significance of Hemoptysis, J. A. M. A. **148**: 1461-1465 (April 26) 1952.

4. Heller, R.: The Significance of Haemoptysis, Tubercle **27**: 70-74 (May-June) 1946.

5. Berkson, J., and Gage, R. P.: Calculation of Survival Rates for Cancer, Proc. Staff Meet., Mayo Clin. **25**: 270-286 (May 24) 1950.

In addition to these 55 patients, 6 other patients were known to be alive two to five years after examination for hemoptysis. Of the 50 patients who were alive at the end of five years after examination, 3 are known to have died subsequently, making a total of 8 deaths. Data pertaining to these cases are given in table 4. The cause of death

TABLE 3.—*Severity of Idiopathic Hemoptysis*

Severity	Women	Men	Total
Blood streaked sputum only (+).....	2	1	3
1 to 30 cc. of blood (++).....	6	15	21
30 to 150 cc. of blood (+++).....	15	21	36
More than 150 cc. of blood (++++)...	3	10	13
Total	26	47	73 *

* Unknown in 2.

was unknown in three cases, and in one case death was due to an unrelated condition. Two patients (cases 3 and 7, table 4) undoubtedly had bronchiectasis, which was not demonstrated at the time of our examination. One patient (case 5) was found to have carcinoma of the bronchus less than one year after our examination, and it must be assumed that this tumor was present at the time of our examination.

One patient (case 6) continued to expectorate blood repeatedly and survived only four years. Postmortem examination revealed only hemosiderosis of the lungs, which was probably secondary to the hemoptysis; nothing was found to explain the bleeding.

The hemoptysis of the 47 living patients before and after examination is compared in table 5. Most of these patients had little or no bleeding in the years following their examinations. We do not suggest that a thorough examination prevents subsequent hemoptysis. A more reasonable explanation is that in the absence of demonstrable disease hemoptysis is not likely to be a recurrent symptom.

COMMENT

Except for those patients who were found subsequently to have pulmonary disease, the cause of the hemoptysis remains unknown. Only 13 of the 75 patients

TABLE 4.—*Summary of Deaths in Cases of Idiopathic Hemoptysis*

Case	Age, Yr.	Degree of Hemoptysis * At Time of Examination	Degree of Hemoptysis * Continued After Examination	Survival After Diagnosis, Yr.	Cause of Death
1	53	++	Unknown	7	Coronary thrombosis
2	57	+++	None	5	Unknown
3	17	+++	+++	6	Bronchopneumonia
4	56	++++	Unknown	3	Unknown
5	52	++	++	4	Carcinoma of bronchus
6	18	++++	++++	4	Hemosiderosis
7	41	+++	+++	4	Bronchiectasis
8	52	++++	++++	2	Unknown

* Graded as in table 3.

had systolic blood pressure of more than 150 mm. of mercury or diastolic pressure of more than 90 mm. With but one exception these 13 patients were more than 30 years old. We doubt that this incidence of hypertension is unusual or that there is any relationship between the hemoptysis and the height of the blood pressure. Four of the female patients reported that the hemoptysis had occurred just before, during, or just after a menstrual period. Some might call this vicarious menstruation; however, these 4 comprise only 20% of the 20 women less than 50 years of age, and chance alone could account for the apparent relationship in this group. None of our 75 patients had blood dyscrasia or evidences of pulmonary hypertension.

Since two of the patients who died probably had bronchiectasis that was not demonstrated, it seems possible that others of this group also had small areas of bronchiectasis. Other possible causes are small ulcerations of the bronchial mucosa and pulmonary infarctions. Recently we have seen patients who complained of gross hemoptysis and in whom these diagnoses were established by thoracotomy and pulmonary resection.

The prognosis for idiopathic hemoptysis seems to vary considerably, depending on whether or not the patient continues to expectorate blood. When the hemoptysis persists, serious disease must be suspected in spite of negative examinations, and further study is advised. Our series indicates that the prognosis is good if hemoptysis does not recur.

TABLE 5.—*Degree of Hemoptysis After Examination Compared with That Before Examination in 47 Living Patients*

Postexamination Hemoptysis	Women	Men	Total
None	9	18	27
Less	6	6	12
Same	4	3	7
More	0	0	0
Total	19	27	46 *

* Unknown in 1.

SUMMARY

A study has been made of the case records of 75 patients who had hemoptysis for which no cause could be detected. Follow-up information five or more years later was available concerning 55 of these. Of the traced patients 90.9% lived five or more years after the date on which the diagnosis of idiopathic hemoptysis was established. Of the eight known deaths in this series, three are known to have been due to primary pulmonary disease. Of these, one was due to bronchogenic carcinoma. It is concluded that the prognosis in idiopathic hemoptysis is good, particularly in cases in which the hemoptysis does not become a recurrent symptom.

Positive Serologic Reactions in Pregnancy.—There is . . . difference of opinion as to the management of the pregnant woman in whom routine and repeated serologic examinations reveal positive reactions. Often it is her first pregnancy; clinical and serologic examinations of her parents and husband are negative and the patient presents no clinical or anamnestic evidence of syphilis. Furthermore, investigations for possible nonsyphilitic diseases known to produce nonspecific serologic reactions may be fruitless. It is not safe to assume that standard serologic reactions are of the false positive type unless they are checked by a negative treponemal immobilization test. It is generally agreed that unless biologic false positivity can be proved, these women are entitled to the protection of a course of penicillin therapy to insure against a prenatal syphilitic infection of the fetus in utero. In order to prevent possible psychic trauma, the woman should be informed that she does not necessarily have syphilis, and that the treatment is not for herself but rather for the protection of her baby.—C. R. Rein, M.D., and G. H. Kostant, M.D., New York, N. Y., Special Diagnostic and Therapeutic Problems in Syphilis, *American Journal of Syphilis, Gonorrhea, and Venereal Diseases*, July, 1952.

IMPACT OF MEDICAL CARE PLANS ON THE MEDICAL PROFESSION

Arthur M. Master, M.D., New York

The purpose of this report is to alert the practitioner of medicine, and through him the public in general, to the terrific impact on private practice in New York City of an insurance scheme that combines prepaid voluntary health insurance and panel practice, that does not permit the patient's free choice of a physician, and that places no income ceiling restriction on the participant. During the five years of the scheme's existence (particularly in the year 1951-1952, at which time I was president of the Medical Society of the County of New York), I have observed the hammer blows of this plan against the private practice of medicine. The county medical society has received innumerable complaints from physicians about this plan. At stated meetings the society has vehemently denounced it. I refer specifically to the Health Insurance Plan of Greater New York, Inc. (also known as H. I. P.).

In my opinion this health insurance plan is undemocratic and unfair in that it receives a monopolistic subsidy from the City of New York. Furthermore, it is not only subsidized by the City of New York to the exclusion of plans that allow free choice of physician but it is also subsidized by employers, by physician members of the plan, by private foundations, and by trade unions. In addition, it is subsidized by at least two hospitals in New York that many physicians believe may be engaging illegally in the corporate practice of medicine. The practitioner of medicine, I repeat, must know about this plan; he must know that not only persons earning less than but also those earning more than $6,500 a year are welcomed into it and that if the scheme progresses there will be no private patients and therefore no private practice. In the end, compulsory health insurance would take over. It is suggested, in order to maintain freedom of choice of physician, that voluntary health plans such as Blue Shield immediately take steps to make their protective coverage base more comprehensive. Further, physicians should energetically help these voluntary health plans so that they may compete with this unfair, undemocratic H. I. P. They must agitate that city tax moneys not be used against the private practitioner. In New York City, as elsewhere, the private practitioner pays taxes too.

At this point some general remarks on prepaid medical insurance plans are pertinent. A striking change in the pattern of medical care in the United States has taken place in the rapid development of these plans.[1] It is apparent that large segments of the middle and lower income groups in this country seek to mitigate the costs of illness by some form of prepayment on an insurance basis. Simultaneously, the trend to the group practice of medicine is growing steadily. Where group practice and prepaid medical care have united in a contractual arrangement denying full, free choice of physician by the patient, a unique situation is created that may seriously threaten the survival of the individual practitioner in private practice. The Medical Society of the County of New York, with a current membership of 7,000 physicians, has had the opportunity during the past five years to study the effects of such a contractual arrangement between a group type of panel medicine and prepaid medical insurance. It seems desirable to set forth some observations concerning this arrangement in order to warn the entire medical profession of what may lie ahead. Physicians everywhere should be aware of what is happening in New York City, for it can also happen in their own communities. Not to be overlooked in the contract linkage between a specific medical group and a specific insurance plan is the restrictive panel type of medicine that is created and under which the free choice of physician is no longer possible. Thus, there has developed in the United States a variation of the earlier, well-known English panel system of medicine that became the forerunner of the present British National Health Service—socialized medicine.

NEW YORK CITY HEALTH INSURANCE PLAN

Choice of Physician.—In the metropolitan area the Medical Society of the County of New York has experienced little difficulty with voluntary prepaid medical care plans of the Blue Shield type, because free choice of physician is possible therein. Payment is made on an indemnity basis at specified fees for services rendered. These fees are paid directly to the patient or, with the patient's permission, directly to the practitioner. In contrast, under a system of comprehensive medical care that operates through a panel of physicians under contract with a specific insurance scheme, such as the Health Insurance Plan of Greater New York, the patient must go only to panel practitioners to receive treatment. He may, of course, go to physicians outside the panel but only at an economic penalty, i. e., the penalty of paying these nonpanel physicians their regular fees. Despite the additional expense, patients in such comprehensive medical care plans as that in New York are sometimes so dissatisfied with the service afforded them that they accept this double cost penalty in order to obtain the physician of their choice.

Basic Fault.—The basic fault of panel medicine is that the physician is paid a per capita fee per year, regardless of how much or how little time he devotes to a patient. Being only human, the panel physician is tempted to run patients through his office on a mass production basis, just as anyone else would do, so as to increase his annual income. In NewYork City there is an additional reason for hurrying the visits of panel patients, for the panel practitioner often has to treat private patients also in

Past president of the Medical Society of the County of New York.

1. (*a*) Voluntary Prepayment Medical Care Plans, rev., Council on Medical Service, Chicago, American Medical Association, 1951. (*b*) Clark, D. A., and others: Health Insurance Plans in the United States, Report of the Committee on Labor and Public Welfare, S. Rept. 359, pt. I, 82nd Cong., 1st sess., May, 1951. (*c*) Hunt, G. H., and Goldstein, M. S.: Medical Group Practice in the United States, Publication 77, Federal Security Agency, United States Public Health Service, 1951. (*d*) Accident and Health Coverage in the United States: Annual Survey, New York, Health Insurance Council, June, 1952.

order to eke out a living. Thus, panel type medicine in New York is demonstrating, as it already has elsewhere, that the intimate physician-patient relationship is lost, that less average time is spent per patient, and that poor medical care often results.

Ultimate Goal.—As I have already indicated, the specific insurance company and medical care plan that the New York County Medical Society has to consider is the Health Insurance Plan of Greater New York, Inc., a nonprofit insurance corporation using group and panel type medical care. It is chartered under Article IX-C of the Insurance Laws of the State of New York. In 1950 THE JOURNAL gave Dr. George Baehr [2] the opportunity to present the purposes and objectives of this plan. When H. I. P. was being planned, its founders envisioned, among other possibilities, that it would be a forerunner of a system of compulsory health insurance by the federal government and would be financed by payroll tax deductions in a manner similar to that provided under the Social Security Act. This provision of the plan is a major step on the road to socialization of medicine.

Membership.—Though the health insurance plan covers only a fraction of the city's population (345,000), every taxpayer in New York indirectly has a stake in the scheme. City funds, up to $3,000,000 in the next budget, are to be used to pay one-half the insurance premium for certain groups of city employees. Such city-financed premium benefits—they have been called "discriminatory" by official resolution of the New York County Medical Society—are not given to other city employees who prefer medical care insurance other than H. I. P. Trade unions have also been a bulwark of the Health Insurance Plan of Greater New York. While the average union member is in the moderate income bracket, it is possible for anyone in the union, regardless of salary, to be covered by the plan and its benefits.

Efforts are now being made to enlist residents of the various large, subsidized, low-cost New York housing projects in the health insurance plan. It is in these huge low-rental projects that H. I. P. is having a major effect upon the private practitioner of medicine. In the past, several physicians usually signed leases for offices in the housing developments. However, since the tenants often subscribe as a group to the panel system of medicine, these private practitioners soon find themselves without patients. They can move away from the housing project and hope that enough residents will come to see them to keep them in practice, or they can move to another section of the city and start anew. Neither alternative is desirable, yet private practitioners are now forced into one or the other of them. As a third choice they could, of course, try to join H. I. P.

Recently, there has been an attempt to organize groups of physicians in the leading hospitals of New York City within the framework of the health insurance plan. The Bellevue Hospital unit has already been established in Manhattan and the Montefiore Hospital unit in the Bronx. Such H. I. P. groups are composed of physicians who have staff appointments at these leading hospitals and who have ready access to their facilities. In such groups the plan has another advantage. These groups use millions upon millions of dollars' worth of equipment and buildings. There is, therefore, no need for the Health Insurance Plan of Greater New York, Inc., itself to accumulate and invest enough money to build its own units and to employ the requisite full-time staffs of physicians. It is as if—to use a not impossible example—H. I. P. were to move to Rochester, Minn., and sell insurance to many thousands of its inhabitants, saying to them, "See, when you join up with us, you are assured of your medical care at the great Mayo Clinic. Without a cent of investment on our part, we have made a deal that allows us, without cost, to use all the facilities of the Mayo Clinic. All you have to do is to pay, regardless of your own income, the small yearly premium." One truly wonders what the medical profession of the Midwest and of the rest of the nation would say if this hypothetical situation actually came to pass. My warning is that in New York City this situation is a stark reality. Incidentally, it is a question whether the hospitals whose staffs are so organized are not illegally engaged in the corporate practice of medicine.

Advertising.—During the past year the anger of the private practitioners of New York City became intense concerning the health insurance plan, because of a series of full page advertisements that appeared in nearly all the leading New York newspapers:

"What Does Your Heart Say?" . . . . . Join H. I. P.
"How Much Does a Baby Cost?" . . . Join H. I. P.

So ran the advertisements, with the implication that somehow the mere joining with H. I. P. freed the subscriber from worrying about his heart or about the cost of having babies. It was then that cries of protest arose and members of the Medical Society of the County of New York asked, "What are you (Mr. President) going to do about it? As physicians, we can't advertise. Why can H. I. P. doctors advertise?" These complainants, and they were many, were answered with the contention that the Health Insurance Plan of Greater New York could advertise, because it was a legal insurance company. Any attempt by the medical society to bar such advertising might go counter to the laws of the state of New York, which do not forbid corporations generally to advertise their wares.

Subsidy.—Now for an examination of the potentials and weaknesses of an organization like the Health Insurance Plan of Greater New York. From such an analysis and from the knowledge thereby obtained, the warning to the medical profession and the private practitioner of medicine will become clearly ominous. The prime strength of H. I. P. is its promise of a medical utopia. It pledges to deliver more medical care per dollar than any other plan. With this battle cry it has "conquered" city fathers, labor unions, executives of management, and housing groups. Competitive medical care plans, like the United Medical Service (Blue Shield), know from their own statistical records and far greater actuarial experience that the apparent fulfillment of H. I. P. promises is contingent on (*a*) subsidy, direct or indirect, and (*b*) poor quality of medical care, or (*c*) "sweatshop" medical personnel. There is no gainsaying the fact that this

2. Baehr, G.: Health Insurance Plan of Greater New York: First 3 Years, J. A. M. A. **143**: 637 (June 17) 1950.

health insurance plan has a powerful appeal, with its expectation of a medical utopia. The scheme truly uses the "best buy for the money" or, as in New York, the "I'll get it for you wholesale" form of sales appeal. To paraphrase a popular slogan of one of the city's great department stores, "Nobody, but nobody, undersells H. I. P."

Despite its rosy promises, however, all is not completely satisfactory in the New York health insurance plan organization. This is evidenced by letters and messages of complaint sent to the county medical society and to its officers. Moreover, many members of the society in their private practice treat plan subscribers who are dissatisfied with the service. Then too, participating physicians themselves become dissatisfied and leave H. I. P. when they find that they help subsidize the plan, not by dollars perhaps, but by their own back-breaking labors. They can tolerate sweatshop medicine just so long.

Another weakness of the Greater New York plan lies in its origins and motives and in the thinking of its founders. It places great stress upon the valuable statistical data that it hopes to collect on medical care. The plan organization does have an entire department collecting statistical experience. One may ask, "Experience for what?" A former official observer of the New York County Medical Society on H. I. P.'s medical control board [3] remarks, "As I see it, the experience being gathered has value only for a plan ultimately to be subsidized by the Federal Government." This conclusion is frankly admitted by the former president of the health insurance plan in an article signed by him in the *New York Times* [4]:

> There are two reasons why the middle course [H. I. P.] is needed at this time. First, the advocates of the Federal plan go too far, as we simply do not have enough experience to devise nationwide compulsory health insurance. The proposed middle way [referring to H. I. P.], it should be noted, does not rule out compulsory health insurance and in effect moves toward it, but meanwhile provides needed experience. Second, the uncompromising opponents of the Federal plan [this was in the era of the proposed Wagner-Murray-Dingell bill] do not go far enough with their plans for voluntary insurance. The opponents of the Federal plan must come around to complete voluntary health insurance rather than the limited form most of them now favor, and they must all be convinced of the need for Federal aid to push such voluntary health plans.

The late Mayor La Guardia of New York was another founder of the health insurance plan and even more frank about its purposes when he stated in a radio address [5]:

> I want to say that a National Compulsory System is preferable to a local voluntary system. The likelihood of the immediate passage of the Wagner-Murray-Dingell Bill is not at all certain. I will say that when it is enacted into law and the proper medical provisions become operative, there will be no need for our City plan [H. I. P.] and we would be only too happy to turn over our experience and call it a day.

One need add nothing more. Here, starkly revealed, is the thinking of the top echelon of H. I. P., their plans, and their goals. Their technique is clear: to start and operate by subsidy. Already they have subsidy in many forms. Over $750,000 has been received by the plan organization from various foundations (the Commonwealth Fund, the Rockefeller Foundation, and the New York Foundation) for "research purposes"—research to gain the statistical experience already mentioned. Subsidy is illustrated by the fact that fees are consistently lower than those of private practitioners. Under the present per capita fee system now employed by H. I. P., a qualified surgical specialist realizes $35 or less for a hysterectomy. This is certainly far below the average surgical fee for such an operation.

Coverage.—An insidious feature of the Health Insurance Plan of Greater New York is that it does not limit its coverage to those who need help in meeting medical bills but includes as well those who are amply able to pay the private practitioner's fee. When it began, H. I. P.—as do all sound medical insurance plans—set a salary ceiling upon its subscribers. This was fixed at a more generous level than in competitive plans, i. e., a $5,000 annual family income level. Soon it was announced that families earning up to $6,500 yearly would be accepted, though at a somewhat higher premium rate. Finally, even the $6,500 ceiling was removed. Now, any employee or any member of a union can join the health insurance plan regardless of his yearly salary. Thus, the president or executive of a large labor union, who may earn several tens of thousands of dollars a year, can obtain the comprehensive coverage of the plan for a premium but little more than that paid by the poorest worker in his union. In corporations, the top executives can obtain the same medical care as the lowest paid office boy for only an insignificant (for the executive) increase in the premium. In a word, H. I. P. now virtually eliminates any question of the ability to pay. Those financially able to pay the most pay but little more than those who can afford to pay the least. The value of this practice as a sales argument to interest the labor leaders and executives in the proposals of the New York plan is not to be overlooked. They obtain what seems to them to be a magnificent "free ride." Since they can greatly influence the vote of the rank and file members to join H. I. P. "voluntarily," one can see the chain reaction of such sales arguments. It is certainly not beyond the realm of possibility that many nationally known organizations have joined the plan because the executives of these organizations were allowed to come in as "free riders."

Lasker Award.—Employers, employees, hospitals, and foundations have probably already been attracted to H. I. P., because this plan received the Lasker Award in 1951. H. I. P. has extensively publicized the honor that the Lasker Award confers and has sought, thereby, to promote its own implied merits. Both the Lasker Foundation, which finances the award, and the American Public Health Association, which judges the recipient and makes the presentation, are laudable organizations. There are, however, two little-known facts that make the value of the award, in this case, questionable: 1. No physician on the selection committee was engaged in the private practice of medicine. All were public health officials or full-time, salaried physicians in large hospitals or

3. Davidson, H. B.: Personal communication to the author.
4. Heyman, D. M.: Health Issue: A Middle Course, Sunday Magazine Section, New York Times, March 6, 1949, p. 10.
5. La Guardia, F. H., Radio address over WNYC, New York, April 30, 1944.

medical schools. While they probably tried to be objective, their primary interest may, subconsciously, have been in a system of medical practice like that of H. I. P., which encroaches so actively on the private practice of medicine. 2. Mrs. Mary Lasker, an officer in the Lasker Foundation, which made the award, is also an officer (the secretary) of H. I. P. Whether objectivity can be obtained by a person who serves in this dual capacity, no matter how sincere she may be, is questionable.

In summary, the case against the Health Insurance Plan of Greater New York reveals that the keystone of its structure is subsidy. Remove the subsidy, the structure falls, and all that is left is a system of very inferior medical care. If the medical profession and the nation are ready to accept medical subsidy for all persons, instead of just for the indigent ones as in the past, let there be an open declaration in acceptance of it. If someone else will pay your medical bills, a comprehensive type of medical service is really a "free ride." Ultimately, however, if everyone obtains the same subsidy, only the federal government (i. e., each and every taxpayer) must pay the bill swollen by a staggering surcharge for the costs of administration. Is that what the nation and the medical profession really want?

ACTIONS TAKEN BY MEDICAL SOCIETIES

Faced with the problems that have been stated, the Medical Society of the County of New York has taken action. On Feb. 25, 1952, the society passed a strong resolution condemning the monopoly position of H. I. P. with the government of the City of New York. The full text of the resolution follows:

WHEREAS: The City of New York, in accordance with a contract with the Health Insurance Plan of Greater New York, Inc., pays 50% of the premium for medical care of its employees, and

WHEREAS: The employees of the City of New York pay the other 50% of the premium for such medical care, and

WHEREAS: The Health Insurance Plan of Greater New York, Inc., has entered into contracts with physicians and groups of physicians (totalling about 1,000) to provide such medical care, and

WHEREAS: There are about 16,000 physicians practising in the City of New York, who pay taxes to the City of New York, and

WHEREAS: The Health Insurance Plan of Greater New York, Inc., does not offer equal opportunity to all these tax-paying physicians to participate in rendering medical care to the City employees, and

WHEREAS: There are other non-profit voluntary health insurance plans operating in the City of New York, in accordance with the laws of the State of New York, i. e., the United Medical Service and Group Health Inc., which are approved by the Superintendent of Insurance and by the County Medical Societies of Greater New York, and

WHEREAS: The said United Medical Service and Group Health Inc. provide for the free choice of physicians, and all physicians in the Metropolitan area may become participating members of these plans, and

WHEREAS: The City of New York refused to pay half of the premiums for health insurance of its employees if they desire coverage by such other approved health insurance plans, and

WHEREAS: The City of New York pays half of the premiums for hospital services to its employees provided through "Blue Cross," the Associated Hospital Service of Greater New York, only if such employees are also subscribers of the Health Insurance Plan of Greater New York, Inc., and

WHEREAS: The City of New York thus penalizes its employees who desire hospital services as are available through Blue Cross, but do not care to be subscribers of the Health Insurance Plan of Greater New York, and

WHEREAS: Employees of the City of New York are penalized as well if they choose their own family physician to render medical care as is available through such other non-profit health insurance plans which provide true free choice of physicians, and

WHEREAS: Injured employees of the City of New York who are entitled to Workmen's Compensation aid are guaranteed free choice of physician under the Workmen's Compensation Laws of this State; and

WHEREAS: The Health Insurance Plan of Greater New York gives freedom of choice of physician only from among those selected and approved by their Medical Control Board, and

WHEREAS: The contract between the City of New York and the Health Insurance Plan of Greater New York, a private corporation, may be rightly viewed as monopolistic and discriminating;

Now, therefore be it resolved: That where the City of New York contributes part or all of the cost for medical expense indemnity or medical services; and/or hospital service; the component groups of subscribers of individual subscribers shall have the right to select for such medical expense indemnity or medical services, and/or for such hospital services, any non-profit medical care and/or hospital care plan, approved by the Superintendent of Insurance of the State of New York, and that the City of New York shall pay one-half of the premium to such pre-payment voluntary health insurance plan and/or hospital service plan; and

Be it further resolved: That the Medical Society of the County of New York apprise the Council of the City of New York of this resolution, and request that appropriate legislation be enacted to correct the inequities here described, and be it further

Suggested: That the representatives of the Five County Medical Societies, comprising the Greater City of New York, be instructed to introduce this resolution to the Coordinating Council of the Fve County Medical Societies for appropriate action.

One may ask what effect the above resolution will have upon the New York City Council. The Medical Society of the County of New York has the power only of persuasion. However, the society went clearly on record, emphasized the need to maintain free choice of physician by the patient, and disclosed the discriminatory nature of the panel type group medicine practiced by H. I. P. under contract as an insurance carrier. The county medical society, along with many other medical societies of New York State, has for several years supported legislation seeking to make it mandatory for every health insurance plan to allow free choice of physician for the patient. One such suggested piece of legislation, the so-called Panken Bill, has never come out of committee.[6] If enacted, the Panken Bill would prohibit the operation of those plans like H. I. P. that allow only panel medicine, without free choice of physician.

Within the New York County Medical Society, the action to be taken in this matter is highly charged with emotionalism, for many of the member physicians belong to health insurance plan groups. In some medical societies, though not in the New York County unit, resolutions have been passed that demand that some practitioner of an H. I. P. group be brought before the Board of Censors and expelled for alleged violation of the Code of Professional Conduct of the Medical Society of the State of New York, under which all state-licensed physicians operate. The advertising by the plan corporation has aroused this angry demand. It may be anticipated that any H. I. P. physician who might be expelled

6. S. 1082, New York State Legislature, 1952 session, introduced by Harold I. Panken.

from his society as a result of such action would take legal action against that society, and the case would eventually come to trial before the courts. Legal opinion varies as to the possible outcome of such court action. In New York County no such drastic action against individual physicians has been instituted.

SUGGESTED PLANS OF ACTION

It is suggested that the growth of voluntary health plans that permit the free choice of physician be enhanced and speeded by wider application of a $100, $200, or $300 deductible clause (somewhat after the manner of automobile collision insurance), which would permit a much lower premium to be paid by the subscriber and would give major coverage for catastrophic illness or operation. Most persons in the middle income bracket can absorb medical costs of minor and routine treatment. It is the catastrophe that creates the economic emergency. There is also merit in the proposals to permit, under federal income tax legislation, a $100 or more deduction for ordinary medical expenses rather than to allow deductions only when the medical expenses are greater than 5% of the gross income.[7] It is an injustice that income taxes are collected upon money spent for sickness. The government may need tax income, but one wonders if the government really needs to tax the individual person on his illness.

Within the medical profession itself, the greatest peril exists until all physicians realize the inroads on private practice that result from the combination of group practice tied by contract to prepaid health insurance plans and not permitting free choice of practitioner. Too many physicians, busy with their own private practice in the manner of a bygone era, are not alert to the problem. They cannot or will not comprehend the changing pattern that H. I. P. and plans like it are forcing upon the profession. They seem still to think that a medical society should be organized solely for scientific purposes and medical education and that it should not consider and act upon the economic and ethical problems that arise. Undemocratic and unfair practices, such as H.I.P.'s possession of a medical care monopoly for the New York City employees, must be eliminated. Widespread publicity should be directed to the attention of physicians and the public to the effect that, with health insurance plans accepting persons with incomes of $6,500 and over, private practice with free choice of physician is being destroyed. The continuation of this procedure means that compulsory health insurance will be the final result.

Blue Shield and similar plans should widen their coverage. The private practitioner must cooperate and be willing to accept lower fees. Medical coverage cost must be made more reasonable for the lower and middle income groups. That this can be done to full satisfaction of patient and physician alike is exemplified by the Windsor plan.[8] The Windsor Medical Services, of Windsor, Ontario, Canada, a voluntary, nonprofit, prepaid medical care plan sponsored by the Essex County Medical Society, has been in operation since 1939. There has been a progressive increase in enrollment, so that by May, 1951, there were 100,000 members listed on its ledgers. It is a comprehensive insurance plan in which more than 95% of the physicians in Essex County Medical Society participate. The physicians are paid on a fixed schedule of fees. The monthly subscription rate varies, according to income, from a single subscriber earning $300 or less to the family subscriber earning $6,500 or less. The monthly premium is $1.85 for a single employee, $3.70 for a man and wife, $5.00 for a family with one child, $6.10 for a family with two children, and $7.00 for a family with three or more children. This successful plan shows what prepaid fee for service could do. That is what Blue Shield should strive for. Compulsory health insurance will then be prevented.[9]

SUMMARY

Voluntary health insurance plans that permit the free choice of physician are welcome and desirable. Group practice of medicine, in and of itself, is desirable. The combination of the two without free choice of physician creates a system of panel medicine that may very well be the forerunner of socialized medical care at the national level. Comprehensive medical care plans, at least in New York City, can operate in only one of three ways or their combination: (*a*) by subsidy that comes from philanthropy or from participating physicians by their willingness to render medical care at substandard fees; (*b*) without subsidy, by giving low grade medical care; (*c*) by "sweatshop" labor of the participating physicians. The advertising used by the Health Insurance Plan of Greater New York may be legal, but it also may be unethical. There seems to be no clear-cut way to resolve this point without a test case in court.

The entire medical profession of the nation should be alerted to the problems here discussed and should be made to see the insidious attack against private practice that results from the combination of group and panel medicine in contractual combination with a nonprofit, prepaid medical care plan without free choice of physicians and without a limit on the income of the subscriber. Voluntary health plans that allow free choice of physician should widen their base and become more comprehensive. The foundations, the hospitals, and the philanthropists should be encouraged by the medical societies to support prepaid medical insurance plans in which free choice of physician is permissible and in which a definite annual limit of family income is set at $5,000 to $6,500. (Beyond these figures the family physician should be paid the difference between his regular fee and the fee allowed by the plan.) Finally, the voluntary life insurance schemes for catastrophic illnesses should be fostered by the medical profession.[10] With deductions for the first $100, $200, or $300 of the cost for illness, the patient could be insured for one year for sums up to $5,000 for his catastrophic illness.

125 E. 72nd St. (21).

7. Master, A. M.: Inaugural Address, New York Med. **7**: 16 (Nov. 5) 1951. President's Page, ibid. **8**: 23 (April 20) 1952.

8. Axelrod, S. J., and Patton, R. E.: The Use and Abuse of Prepaid Comprehensive Physicians' Services, Am. J. Pub. Health **42**: 566 (May) 1952.

9. Campbell, R. R., and Campbell, W. G.: Compulsory Health Insurance: The Economic Issues, Quart. J. Economics **66**: 1 (Feb.) 1952.

A FLUID AND ELECTROLYTE BALANCE SERVICE FOR CLINICAL USE

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The importance of proper management of fluid and electrolytes in seriously ill patients in the prevention of morbidity and mortality due to electrolyte imbalance has been adequately stressed in the recent large volume of literature on this subject. Because the evaluation of the condition of patients with serious fluid or electrolyte imbalance involves a complete understanding of the intricacies of fluid physiology, it would obviously be of great value to have some system of preventing such imbalances that would not require a deep understanding of the subject on the part of physicians. The idea for such a fluid balance service is not new or original, and it has been used in various forms at several large medical centers. The fault of some of these plans, although simple in procedure, lies in the fact that they require a fine understanding of the subject and, in other than ordinary situations, may give misleading information as to sodium and potassium loss. The following plan has been in use at a private hospital, with good success in simplifying the fluid maintenance of seriously ill patients at a nominal cost to the patient. The method assumes the availability of a flame photometer for the determination of sodium and potassium in urine and in intestinal secretions. The importance of the flame photometer to the modern routine laboratory is now well accepted, and accurate understanding of the state of balance of a patient with respect to electrolytes is difficult without such help. I do not mean by this to minimize the importance of the history and physical findings in indicating the state of hydration and the degree of salt and potassium depletion.

OPERATION OF THE FLUID AND ELECTROLYTE SERVICE

When fluid and electrolyte balance service is requested by the physician, the chemistry laboratory (which assumes direction of the service) attaches a placard over the head of the bed to identify properly the patient as being on strict balance orders. Graduated bottles (discarded intravenous infusion bottles) labeled "drinking water" and "irrigation fluid" are left at the bedstand and renewed daily. Labels are also applied to urine collection bottles and to negative suction and drainage bottles, and a placard is placed over the toilet to warn against emptying of bottles by nurses and aides. Patients scheduled for surgery are tagged so that fluids given at operation may be recorded (fig. 1). A simple set of mimeographed instructions is left with private nurses, if any, and general floor duty nurses are instructed as to fluid and electrolyte balance procedure. These instructions briefly explain the importance of the service and point out that only fluids from the marked bottles are to be used for drinking or to irrigate tubes, and no other source of fluid supply is to be used. All bottles for intravenously given solution used each day are left under the patient's bed, including separate ampules of potassium chloride.

Each morning the fluid and electrolyte balance service cart (fig. 2) is wheeled to the patient's room, and the tabulation is made of fluid and electrolyte intake from the labeled graduate drinking water and irrigation bottles and from the bottles with solution for intravenous administration and potassium ampules under the patient's bed. Tabulation of output is made from volumes of urine and other drainage, and a 5% or 10% aliquot is taken from each source and mixed for electrolyte determination later. For this purpose graduate cylinders and collection bottles are carried on the fluid and electrolyte balance cart. If gross blood is visible in any secretion, the aliquots are not combined, and each specimen is run separately, the bloody specimen being so marked, because of the effect of hemolysis on potassium determinations. After electrolyte determinations have been made, the total sodium and potassium output in the 24-hour period is recorded. On the first or second day of the service, blood is drawn for determination of serum sodium, chloride, potassium, and carbon dioxide combining power. This is done to serve as a base line for future deviation of blood chemistries and, more important, may indicate imbalances already existing in sick patients who may have become depleted in the several days prior to admission to the hospital.

The fluid and electrolyte balance service begins on the morning of operation in most surgical cases, and whenever ordered for medical patients, and continues as described above for a total of three days. This period of three days was arbitrarily picked because by this time most patients are over the acute postoperative shock and, in most cases, suction tubes have been removed. If further fluid and electrolyte balance service is desired, it is requested for a second three-day period. Since an extension of the service ordinarily indicates a more precarious state of balance in the patient, serum chemistry determinations are done every other day in the second fluid and electrolyte balance study period, or oftener if so desired by the physician.

For tabulation of results a special sheet is used (fig. 3), which also serves as the routine intake and output sheet for all hospital patients. On this the total fluid intake and output are listed and totaled, and a minus or plus difference is recorded. The intake of electrolytes is recorded from the intravenously or orally administered fluids, and the output is recorded from urine and drainage fluid after electrolytes have been determined on the flame photometer. A plus or minus balance is then recorded. This sheet is left on the patient's chart. The physician has then only to make up the deficiencies of fluid, sodium, and potassium of the day before, or omit it if an excess has been given.

From the Department of Medicine, Menorah Hospital Medical Center and the University of Kansas School of Medicine.

INDICATIONS FOR FLUID AND ELECTROLYTE BALANCE STUDY

It is important to understand that the primary function of fluid and electrolyte balance study is to prevent the development of fluid or electrolyte imbalances; the studies should therefore begin at the time of surgery for

Fig. 1.—Indentification of fluid balance service. Gummed labels are used to mark the various bottles. Discarded intravenous fluid bottles are used for the drinking water and irrigation fluid container. Shown above are the placard placed over the bed, the label for over the toilet, and the tag that is attached to patients prior to surgery.

patients who are to be subjected to intestinal or other severe procedures that will necessitate suction tubes, fistulas, or prolonged intravenous feeding. If fluid and electrolyte balance study is started after the water, salt, or potassium depletion has developed, it will show only the current daily imbalance and will not indicate the cumulative total deficit of electrolyte or fluid, except as reflected

Fig. 2.—Fluid and electrolyte balance service in operation. The cart has a plastic surface and is used to carry the bottles of drinking water and irrigation fluid. The wooden tray on the cart has compartments for the aliquot bottles and, by means of half-circles cut in the tray ends, carries three graduated cylinders for measurement of urine and drainage volumes. Syringes, needles, test tubes, and alcohol sponges are also on the cart for drawing of blood samples.

in the blood chemistry. It has been adequately shown that the serum level of sodium or potassium does not in itself indicate the qualitative or quantitative deficit of the substances in the body as a whole. The value of fluid and electrolyte balance study in patients with cardiac and nephritic disease subjected to surgery is particularly evident, since it is important to keep sodium intake to a minimum and yet avoid the danger of salt depletion.

EXPERIENCE WITH FLUID AND ELECTROLYTE BALANCE SERVICE AND COST

Once the routine of fluid and electrolyte balance service was established, it was found to operate smoothly and efficiently. The collection, measurement, and recording of results for 10 patients requires about three hours of an efficient technician's time. The procedure has been well accepted by surgeons and physicians and has lightened the work of floor nurses in maintaining accurate fluid charts, which in most cases is difficult and of limited

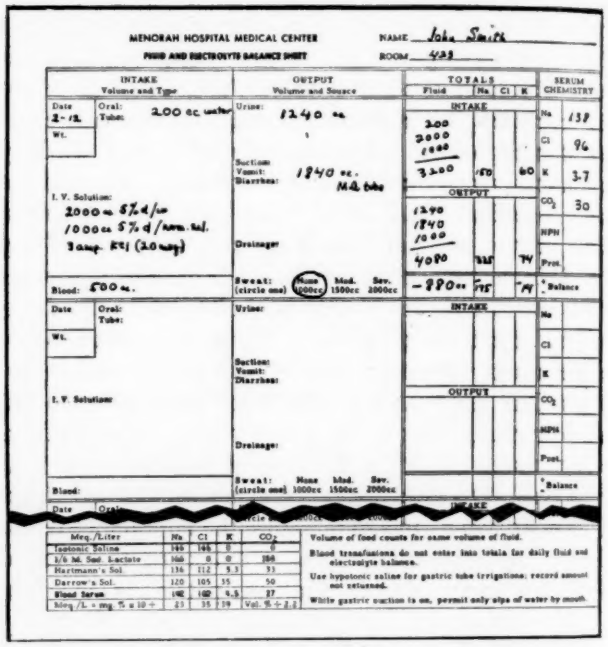

Fig. 3.—Daily fluid balance sheet. The chart size sheet has space for three days' tabulation (the space for one day has been removed in the above cut). A representative day's tabulation is shown. The information at the bottom of each sheet is a quick reference for composition of various fluids given intravenously compared with blood serum. The physician has only to order the amount of fluid and electrolyte necessary to make up the balance deficit the following day, in addition to ordering the current day's expected requirement.

value because of inexperienced floor aides and changes of shifts in personnel. The cost to the patient has been set at $27 for each fluid and electrolyte balance service period of three days. This reasonable rate was made possible because of the volume of work and because it is considered a necessary and important hospital service that would be denied to patients if the cost were prohibitive.

SUMMARY

The description and operation of a fluid and electrolyte balance service in a small private hospital is presented.

ADDENDUM

Since this article was submitted for publication, we have added to the fluid balance sheet shown in figure 3 a table indicating average amounts of sodium and potassium that may be lost in sweat after the first few postoperative days.

1406 Bryant Bldg. (6).

APPRAISAL OF TOPICAL USE OF ANTIHISTAMINES

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and
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The era of antihistaminic therapy was instituted in 1933 when Fourneau and Bovet [1] demonstrated that certain phenolic ethers had the property of counteracting the action of histamine in vivo and in vitro. Their most effective compound, 929 F, as well as compound 1571 F, studied by Staub,[2] were so toxic to humans as to preclude their therapeutic usage. In 1942 Halpern [3] reported his studies with compound 2339 RP (antergan® [dimethyl-amino-ethyl-benzylamine]), which proved to be well tolerated. Since then numerous antihistamines have been synthesized, studied, and made available for oral, parenteral, and topical use.

The rapid succession of "new and better" antihistamines made appraisal of their value difficult and prompted a report by the Council on Pharmacy and Chemistry of the American Medical Association entitled "Too Many Drugs?" [4] Reports relating to the chemistry and pharmacology of the antihistamines and to the results of oral administration are plentiful and have been well summarized by Feinberg and others.[5] We will confine this report to the clinical results obtained by the topical application of the various antihistamines and will summarize herein the replies of 200 dermatologists to a questionnaire regarding their experiences with this type of therapy.

PREVIOUS STUDIES

Ethylenediamine Derivatives.[6]—Tripelennamine (pyribenzamine® [Ciba]) hydrochloride: Feinberg and Bernstein [7] found that the topical application of 2% tripelennamine hydrochloride in water soluble or anhydrous base ointments afforded relief of itching in 24 of 33 patients with atopic dermatitis and in 8 of 9 patients with pruritus ani. Sulzberger and co-workers [8] treated 90 patients with tripelennamine cream. Allergic, contact-type, eczematous sensitization confirmed by patch test occurred in two of them. Sulzberger and co-authors concluded that 2 to 5% tripelennamine hydrochloride cream was a good, clean, nonstaining ointment useful in the treatment of lichen simplex chronicus. They were unable to confirm Feinberg's [7] beneficial results in atopic dermatitis and pruritus ani. Waldriff and associates [9] included 141 patients treated with tripelennamine topically in their series. Thirty-three of these received good to excellent results, and 50 fair results. It appeared to be most useful in circumscribed neurodermatitis, for which 23 of 29 patients attained at least fair results. In the total series (141 patients) there were 10 reactions.

Thenylpyramine ("histadyl" [Lilly]) hydrochloride or methapyrilene (thenylene® [Abbott]) hydrochloride: Bereston [10] used thenylpyramine hydrochloride cream and reported temporary relief of pruritus in 40% of 104 patients with dermatoses in which the cardinal symptom was pruritus, but few permanent or lasting results were observed. No cases of contact dermatitis were seen. Epstein and Macaulay [11] stated that 2% thenylpyramine hydrochloride cream was a valuable adjunct to topical therapy of various forms of allergic dermatoses, especially lichen simplex chronicus. Occasionally the ointment base seemed to work as well. No sensitization was encountered. Waldriff and co-workers [9] employed both thenylpyramine and methapyrilene topically. With the former, 26 of 58 patients with various pruritic dermatoses were evaluated as showing good to excellent results, while, with the latter, 26 of 63 patients showed similar results. In their series, two patients using thenylpyramine and four using methapyrilene showed reactions. Using an ointment consisting of 2% methapyrilene hydrochloride with 10% calmitol® in a water miscible base ("calthenamine") for the treatment of 75 patients suffering from pruritus, Combes and others [12] termed the results excellent in most cases of urticaria, localized neurodermatitis, and dermatitis venenata, while fair results were noted in about half of the patients with disseminated neurodermatitis and anogenital pruritus.

Pyranisamine (neo-antergan® [Merck]) maleate or mepyramine ("antisan") maleate: Twenty patients with pruritus ani were treated with 2% mepyramine maleate cream by Rasmussen.[13] Results were excellent in 12, good in 3, and of no benefit in 5 patients. He stated that the cream was also good in neurodermatitis and Besnier's prurigo but was badly tolerated in exudative eczema.

Ethanolamine Derivatives.—Diphenhydramine (benadryl® [Parke-Davis]) hydrochloride: This is the first antihistamine prepared in this country.[14] Its topical use was reported by Perry,[15] who, in a study of 22 patients with various pruritic dermatoses, found that 6 patients had moderate and 2 excellent relief from the pruritus, 4 of whom had the same degree of relief from the ointment base alone. McGavack and associates [16] used

From the Department of Dermatology, University of Maryland School of Medicine.

Read before the Section on Dermatology and Syphilology at the 101st Annual Session of the American Medical Association, Chicago, June 10, 1952.

Because of space limitations, some of the bibliographic references have been omitted from THE JOURNAL and will appear in the authors' reprints.

4. Too Many Drugs?, report of the Council on Pharmacy and Chemistry, J. A. M. A. **139**: 378 (Feb. 5) 1949.

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8. Sulzberger, M. B.; Baer, R. L., and Levin, H. B.: Local Therapy with Pyribenzamine Hydrochloride, J. Invest. Dermat. **10**: 41-42 (Feb.) 1948.

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12. Combes, F. C.; Canizares, O., and Di Cyan, E.: Modified Antihistaminic Ointment: Its Topical Use in the Treatment of Pruritis, Ann. Allergy **8**: 493-495 (July-Aug.) 1950.

16. McGavack, T. H.; Schulman, P. M.; Schutzer, R., and Elias, H.: Effect of Topical Applications of Diphenhydramine Hydrochloride (Benadryl), Arch. Dermat. & Syph. **57**: 308-318 (March) 1948.

diphenhydramine ointment in treating 74 patients with itching dermatoses. With 5% diphenhydramine hydrochloride in wool fat and petrolatum, 32 of 56 patients had complete relief from itching, 16 had partial relief, and 8 were not affected. With 2% diphenhydramine in polyethylene glycol (carbowax®) 1500, 12 of 18 patients had complete relief, 2 partial relief, and 4 no relief. The 2% cream was used by Philip [17] in the treatment of 85 patients with various itching dermatoses, and good results were obtained in neurodermatitis, atopic eczema, contact dermatitis, and rhus dermatitis. Waldriff and co-workers [9] reported good to excellent results in 11 and fair results in 17 of 44 patients with various pruritic eruptions. There were two reactions. Orecklin,[18] after using 2% diphenhydramine ointment on 268 patients, concluded that it was of value for relief of pruritus in a variety of dermatoses and that this medication should be of special assistance to those who treated patients with dermatological diseases. In 2% of patients in his series, signs of sensitization or irritation appeared.

Doxylamine (decapryn® [Merrell]) succinate: In their comparative study, Waldriff and associates [9] treated 37 patients with topically applied doxylamine. The results were judged to be good to excellent in 16 and fair in 10 of the patients. One reaction was encountered.

Monamine Derivatives.—Prophenpyridamine (trimeton® [Schering]) maleate: Waldriff and co-workers [9] also treated 90 patients with 2% prophenpyridamine cream. Results were good to excellent in 46 and fair in 23 patients of this group. Two patients exhibited reactions. A series of 50 patients were treated for pruritus accompanying certain allergic dermatologic conditions with 5% prophenpyridamine topically by Wittich.[19] The bland base ointment was used as control. Very satisfactory results were noted in a majority of cases of urticaria, atopic dermatitis, localized neurodermatitis, and contact dermatitis. In one case of atopic dermatitis and two cases of contact dermatitis, the ointment increased the irritation.

Miscellaneous Compounds.—Phenindamine tartrate (thephorin® [Hoffman-La Roche]): Wooldridge and Joseph [20] reported the results obtained by the use of phenindamine tartrate orally and locally in the treatment of 23 patients with disseminated neurodermatitis. Seventeen (74%) showed more than 50% clearing in from one to seven weeks. One patient became worse, but patch tests were negative. It was the opinion of the two specialists that the oral administration could be omitted without materially affecting the results. Shelmire [21] used 5% phenindamine ointment in a series of 305 patients with pruritic dermatoses. Of these, 233 patients (76.4%) showed benefit from the application of the salve, while only 1 patient showed contact-type sensitization. Shelmire indicated, however, that the sensitizing index is higher than these figures show, since, in an additional 150 patients treated with the ointment but not included in this report because of an insufficient observation period, five additional cases of contact dermatitis due to phenindamine were encountered. Thus, six instances of contact-type sensitization were seen in a total of 455 patients, an incidence of 1.31%. In our series [22] of 50 patients treated locally with 5% phenindamine ointment, 14 (28%) became worse, of whom 5 (10% of the total) were proven sensitive to the drug; the remaining 9 for various reasons were not tested for sensitivity. According to Laymon and Schmid [23] 5% phenindamine applied topically is an effective antipruritic agent in circumscribed neurodermatitis and anogenital pruritus with lichenification, but the results are not encouraging in disseminated neurodermatitis. They stated that it is of value in dry lesions but is more likely to produce irritation on exudative lesions. Laymon and others,[24] in an effort to determine the frequency of eczematous sensitization following the topical application of phenindamine, performed patch tests on 324 patients who had been using the ointment for up to 10 months. Sensitization was present in 1.5% of the subjects. D'Avanzo [25] believes phenindamine ointment is of very little use in disseminated neurodermatitis but is of therapeutic value in circumscribed neurodermatitis. There were no good or excellent results in the former, while there were 39% good to excellent results in the latter condition. Four of 74 patients became sensitized. In a series of 200 patients with pruritic dermatoses treated with phenindamine topically by Stritzler,[26] results were satisfactory in 67.5%. In his review of 1,300 recorded cases in which phenindamine had been used, the index of sensitization was about 2.4%. Madden [27] reported that 141 patients with various selected dermatoses were treated with phenindamine ointment for the relief of itching. Ninety per cent experienced relief or complete stopping of the itching, 5% showed no effect, and 5% had aggravation of the pruritus and dermatitis. He believed phenindamine ointment to be by far the best single agent he had used for the relief of itching in the type of cases studied. Reiss and Kern,[28] in their treatment of 161 patients with phenindamine locally, found that side-effects necessitating discontinuance of the medication occurred in 5.6% of those treated with the salve. However, the reactions were of a serious nature in only 2.5% of the entire series, and the sensitizing index of phenindamine ointment was found to be as low as 0.6%. They concluded that the comparatively high incidence of success (74.5% were helped) and the low sensitizing index warrant the keeping of phenindamine ointment in the dermatotherapeutic armamentarium. Baldridge [29] compared the antipruritic effect of 5% phenindamine in polyethylene glycol 1500 or vanishing cream base with that of the unmedicated base and found no significant difference. The development of sensitivity to phenindamine ointment in a considerable number of patients indicated to the author that further study of the preparation was inadvisable.

18. Orecklin, L.: Control of Pruritus with Diphenhydramine (Benadryl) Hydrochloride Ointment, Arch. Dermat. & Syph. **60**: 629-631 (Oct.) 1949.

20. Wooldridge, W. E., and Joseph, H. L.: Thephorin in the Treatment of Disseminated Neurodermatitis: Preliminary Report, J. Invest. Dermat. **11**: 93-94 (Aug.) 1948.

21. Shelmire, B.: Topical Treatment with Thephorin, Postgrad. Med. **4**: 443-446 (Nov.) 1948.

22. Ellis, F. A., and Bundick, W. R.: Reaction to the Local Use of Thephorin, J. Invest. Dermat. **13**: 25-28 (July) 1949.

26. Stritzler, C.: Studies on Topical Thephorin Therapy: Index of Sensitization and Effectiveness as an Antipruritic, J. Allergy **21**: 432-441 (Sept.) 1950.

28. Reiss, F., and Kern, A. B.: Clinical and Experimental Evaluation of Thephorin Ointment, J. Allergy **21**: 160-168 (March) 1950.

30. Ayres, S., III, and Ayres, S., Jr.: Chlorcyclizine Hydrochloride Ointment in Pruritic Dermatoses, A. M. A. Arch. Dermat. & Syph. **64**: 207-208 (Aug.) 1951.

Chlorcyclizine hydrochloride (perazil® [Burroughs Wellcome]): Ayres and Ayres [30] used 1% chlorcyclizine hydrochloride in a greaseless ointment base for over one year in the treatment of several hundred patients with many different types of pruritic dermatoses. It gave a satisfactory degree of relief in many cases, especially in lichen simplex chronicus and in pruritus ani, vulvae, and scroti. The preparation was frequently not tolerated on raw, moist, or eroded surfaces; however, not a single case of contact sensitization was observed.

PRESENT STUDY

The search continues for the ideal antipruritic that will effectively and consistently relieve the sensation of itching while producing relatively few or no untoward side-effects. A review of the literature indicated that the topical application of the antihistaminics in pruritic dermatoses frequently affords relief. Is their routine therapeutic use warranted, in view of the number of instances of irritation and/or contact-type sensitivity? We believe the antishistamines in medications prepared for topical use have been available for a sufficient length of time for an appraisal of their value, and in order to obtain a consensus of opinion, a questionnaire was sent to 265 dermatologists in the United States and Canada. Two hundred satisfactory replies were received.

COMMENT

While 94% of the dermatologists questioned had employed the antihistamines topically at one time, only 60% still do, and less than 10% use them often. Their use had been discontinued or restricted, because 38% found them ineffective, 22.5% observed a too frequent aggravation of the dermatosis, and 50.5% noted the high incidence of contact-type sensitization to the topical preparations.

An attempt was made to determine which drugs were more likely to cause a contact dermatitis. Five per cent of the physicians had encountered no such reactions; about 17% said any or all may do so. Of those who mentioned specific drugs, phenindamine tartrate (thephorin®) was by far the most frequently incriminated. However, since the drug was also considered to be the most useful and was probably more frequently used, this cannot be considered as conclusive evidence that phenindamine has a higher sensitizing index than the others. Similarly, it should be noted that the six antihistamines most frequently mentioned as causing contact dermatitis (the only ones to be listed more than once) are also the six most frequently named as being most useful, although not in the same order. The popularity and extent of use of the drug determines, in part at least, the number of sensitivity reactions. Phenindamine ointment and tripelennamine (pyribenzamine®) hydrochloride ointment were once each stated to be primary irritants. Eighty-three of the 200 replies included an estimate of the frequency of contact-type sensitization. The answers varied all the way from 0 to 50%, with an average of 8.8%.

On the basis of replies received, about one-fourth of the dermatologists consider the local use of antihistamines to be of value, one-third are undecided as to their value, and almost two-fifths (38.5%) believe they are useless. In answer to the question of whether the preparations of antihistamines for local use should be taken off the market, 29% said definitely "yes" and 37% replied "no." The other physicians were undecided or stated that only certain ones should be removed from sale, while some believed they should be available only on prescription. The latter suggestion has merit. The answers regarding the most frequent sensitizer paralleled those listing instances of contact dermatitis.

Questionnaire to Dermatologists on Topical Use of Antihistamines: Analysis of 200 Replies

Part A

Question	Answer	No. of Answers
1. Have you ever used antihistamines topically?	Yes	188
	No	12
2. Do you use them now?	Often	19
	Occasionally or rarely	101
	Never	80
3. Why did you discontinue their use?	Ineffective	76
	Dermatitis worse	45
	Allergic contact dermatitis developed	101
	(No answer)	56
4. Which are most likely to cause contact dermatitis?	Thephorin®	109
	Pyribenzamine®	47
	Benadryl®	42
	"Histadyl"	24
	Perazil®	4
	Trimeton®	2
	Antistine®*	1
	Thenylene®	1
	Neohetramine®†	1
	None	10
	All or any	35
	(No answer)	29
5. What is your estimate of the frequency of contact dermatitis caused by antihistamines?	0.0%	9
	1.0%	12
	2.0%	10
	5.0%	15
	10.0%	22
	20.0%	10
	30.0% or more	5
	(No answer)	117

Part B

1. Do you consider the local use of antihistamines to be of value?	Yes	49
	Questionable	67
	No	77
	(No answer)	7
2. Do you feel that antihistamines for local use should be taken off the market?	No	74
	Yes	58
	Questionable	42
	Only thephorin®	7
	Available by prescription only	5
	All except perazil®	1
	Only "histadyl"	1
	(No answer)	12
3. Which is the most frequent sensitizer?	Thephorin®	68
	Pyribenzamine®	22
	"Histadyl"	14
	Benadryl®	11
	No difference	32
	None	16
	Unable to say	22
	(No answer)	26
4. Which is the most useful?	Thephorin®	45
	Perazil®	17
	Benadryl®	16
	Pyribenzamine®	11
	"Histadyl"	8
	Trimeton®	4
	Chlor-trimeton®‡	2
	Diatrine®§	2
	Neo-antergan®	2
	"Caltbenamine"	2
	Thenfadil®‖	1

* Antazoline (antistine®) hydrochloride.
† Thonzylamine (neohetramine®) hydrochloride.
‡ Chlorprophenpyridamine (chlor-trimeton®) maleate.
§ Methaphenilene (diatrine®) hydrochloride.
‖ N,N-dimethyl-n'-(3-themyl)-N'-(2-pyridyl) ethylenediamine (thenfadil®) hydrochloride.

As previously mentioned, the list of the most useful antihistamines is similar to that which records sensitivity reactions. It thus appears, if this trend continues, that the more frequently one of these medications is used the more frequently will reactions occur. On the basis of replies tabulated, chlorocyclizine hydrochloride (perazil®) appears to have a low sensitizing index. This may be due to the fact that at the time of circulation of the questionnaire chlorocyclizine ointment had but recently been

made generally available. After it has been used for a longer period of time, more instances of contact dermatitis may perhaps be seen. Such was our experience with phenindamine.[22] Moreover, Epstein and Macaulay,[11] in their report on thenylpyramine (histadyl®) hydrochloride cream stated they had not seen a case of sensitization; however, Epstein [31] subsequently said that "the printer's ink was hardly dry on our paper before we saw the first case of contact dermatitis from this cream; shortly after, we observed another case." In addition, one of the authors of an early enthusiastic report on the topical use of one of the antihistamines stated in his reply to our questionnaire that he had discontinued its use. It is to be noted that Ayres and Ayres did not use chlorocyclizine as the only mode of therapy in most cases but in conjunction with other appropriate treatment. Perhaps some of the less known antihistamines of today or some antihistamines developed in the future may prove to be efficacious and to have relatively low sensitizing properties so that they may be of value in the local treatment of skin diseases.

We neglected to request those dermatologists who believed that the local use of the antihistamines was of value to indicate the conditions in which they found these medications useful. Some physicians volunteered this information. The most frequently named diseases were localized neurodermatitis and anogenital pruritus. Some mentioned that they prescribed the drugs for use in small areas only or for short periods of time. Some also indicated that their use on moist areas should be avoided.

SUMMARY

The literature concerning clinical results attained by topical application of various antihistamines is reviewed, and the replies of 200 dermatologists to a questionnaire concerning their experience with this therapy are summarized. The replies indicate: 1. Ninety-four per cent of the dermatologists had tried the topical use of the antihistamines, but only 60% still use them, and less than 10% prescribe them often. 2. Those who discontinued or restricted their use did so because they believed this form of therapy was ineffective, tended to aggravate the dermatoses under treatment, or resulted in too high an incidence of contact-type sensitization. 3. Phenindamine tartrate (thephorin®) caused the highest number of instances of contact dermatitis; it was also most frequently mentioned as being the most valuable of the antihistamines. There was a close correlation between the lists of those antihistamines causing contact dermatitis and those considered to be most valuable; that is, the frequency of reactions seemed to increase as the popularity of the medication increased. 4. The over-all sensitizing index may be as high as 8.8%. 5. About one-fourth of the dermatologists considered the local use of the antihistamines to be of value, being of most value in localized neurodermatitis and anogenital pruritus and of least value in moist areas. Some physicians place restrictions on the extent or duration of the application. 6. Restriction of their sale by prescription only is advisable.

8 E. Madison St. (2) (Dr. Ellis).

31. Epstein, S., in discussion on Waldriff, Davis, and Lewis.[9]

PSYCHOSOMATIC DISORDERS AND THE NONPSYCHIATRIST

Bernard I. Lewis, M.D., Iowa City

The current interest in so-called "psychosomatic medicine" has evoked many diverse responses from the general medical public. As with any new, or supposedly new, concept, there has been an initial wave of overenthusiasm opposed by a reef of rigid skepticism. The future may possibly reveal the truth to lie somewhere between these conflicting views. At present, however, there persists in many quarters much confusion regarding the incidence, mechanisms, diagnosis, and management of psychosomatic problems. In this presentation the prevailing opinion on these features will be briefly considered and various suggestions offered that may have practical value for the nonpsychiatrically trained physician.

The actual incidence of ill health brought about wholly or in part by psychological factors is unknown. An approximation may be obtained, however, from the data presented in the following table. These analyses were made by several sets of observers on unselected medical patients of varying socioeconomic background. The first three groups were composed of private patients from urban environments, most of whom fell into the higher economic brackets. Hamman's [1] cases were from his personal consultation practice; Allan and Kaufman [2] utilized their Lahey Clinic material; and my subjects were routine unselected patients from the private outpatient service of the Johns Hopkins Hospital.[3] The remaining groups occupied more variable strata. Roberts and Norton [4] studied a lower income group from the medical outclinic of the New Haven Hospital. My second series [5] embraced both private and indigent, rural and semirural patients from the university hospitals in Iowa City. Robinson [6] evaluated in great detail medically indigent patients from the outclinics of the Johns Hopkins Hospital. As the data indicate, the incidence of these disorders, whether entirely or partially psychological in origin, ranged between 34 and 80%. When combined into one large group, nearly one-half (949, or 47%) of the total number of patients (2,038) are seen to have been disabled in some degree

From the Department of Internal Medicine of the State University of Iowa College of Medicine.

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1. Hamman, L.: The Relationship of Psychiatry to Internal Medicine, Ment. Hyg. **23**: 177 (April) 1939.

2. Allan, F. N., and Kaufman, M.: Nervous Factors in General Practice, J. A. M. A. **138**: 1135 (Dec. 18) 1948.

3. Lewis, B. I.: A Psychomedical Survey of a Private Outpatient Clinic in a University Hospital, Am. J. Med., to be published.

4. Roberts, B. H., and Norton, N. M.: Prevalence of Psychiatric Illness in a Medical Outpatient Clinic, New England J. Med. **246**: 82 (Jan. 17) 1952.

5. Lewis, B. I.: Unpublished data.

6. Robinson, G. C.: The Patient as a Person, New York, the Commonwealth Fund, 1939.

as the result of disturbed psychic function. From these reports "psychosomatic disease" would appear to be widely prevalent and to have little regard for socioeconomic class distinctions. Practitioners must be equipped, therefore, to contend efficiently with these nebulous, controversial, but ubiquitous sources of ill health.

Incidence of Psychic Disorders in Medical Patients Noted by Various Observers

Author	No. of Patients	Psychogenic, %*	Mixed, %†	Total, %
Hamman, L.	500	23	11	34
Allan, F. N., and Kaufman, M.	1,000	27	13	40
Lewis, B. I.‡	163	49	27	76
Roberts, B. H., and Norton, N. M.	50	58	22	80
Lewis, B. I.§	151	20	41	61
Robinson, G. C.	174	36	30	66
Combined Totals	2,038	29 (590)	18 (359)	47 (949)

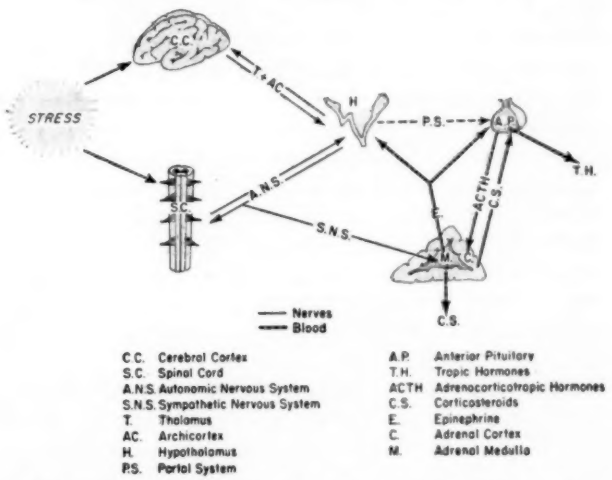
* Illnesses due in their entirety to psychological factors.
† Illnesses due to both psychic and somatic factors.
‡ First series.
§ Second series.

PSYCHOPHYSIOLOGICAL MECHANISMS

In our daily living there is abundant evidence that all feelings—pleasant and unpleasant, expressed and hidden—have their associated physiological reflections. Accepted as commonplace are the suffusion of anger, the blanching of fear, and the blush of embarrassment. Nevertheless, these and various visceral changes that may occur at the same time are of potential medical import. For example, the physical assault of one's defenseless child will characteristically arouse violent anger and initiate a headlong rush to its defense. This emotional reaction instantaneously precipitates diffuse physiological changes that include, among others, an outpouring of epinephrine, tachycardia, rapid conversion of liver glycogen to glucose, and the diversion of blood to skeletal muscles and other vital areas (leaving the splanchnic bed, including the kidneys, relatively ischemic). Thus, the bodily forces are mobilized for battle and the person's immediate needs rapidly served. When the stressful situation is appropriately handled, the emotional and related physiological forces are promptly dissipated, with internal reequilibration at the prestress level.

Harold Wolff [7] regards such psychophysiological responses as purposeful measures and has termed them "protective reaction patterns." His analysis extends beyond Cannon's concept of "fight or flight" and considers the various bodily alterations in the light of their associated emotional states. With his colleagues he has demonstrated a number of psychically-linked patterns that may be characterized by diffuse or focal physiological alterations and may involve any or all organs and tissues. Some prepare the person for offensive activity, while others are defensive, subserving regressive behavior. Structures may be stimulated to overactivity in one setting, yet in another their function may be reduced to virtual standstill. Although variegated in nature and intensity, the fundamental purpose of these protective devices is to equip the person for action. In our modern culture they have become displaced and tend to be provoked by symbols of danger more often than actual assault. This commonly occurs when the symbols are associated, consciously or unconsciously, with previous sensitizing experiences. Reactions thus initiated are frequently excessive and inappropriate to the current inciting stimulus. They may be at odds with approved behavior and require inhibition, or they may function below the level of awareness and be repressed. Typically, the psychopathological stage is set when emotional problems, via unconscious mechanisms, arouse deep-seated drives and desires that cannot be consciously accepted or fulfilled. Consequently, the person is physiologically geared for action that he will not or cannot take. While such psychic forces continue, the associated physiological responses will also persist. Protective reaction patterns, intended originally for actual emergencies, may thus be evoked by symbolic threats and perpetuated into chronic states. In time, the various organs and tissues involved (e. g., the overworked cardiovascular system or ischemic kidney) will reflect this prolonged strain. At first, disturbances of function will occur, but, eventually, structural damage may result.

Although the centers and pathways mediating these processes are not fully understood, the nervous and endocrine systems appear to play the principal roles. The major components of this "neuroendocrine axis" are depicted graphically in the accompanying figure. Noxious stimuli, by common usage termed stress, are quickly detected by the perceptive nervous system. Messages, from the cerebrum above (via interconnecting thalamic and archicortical tracts) and the peripheral autonomic pathways below, rapidly impinge on the hypothalamus. This master autonomic switchboard is centrally placed in the figure to emphasize its dynamic integrating functions. When activated it issues commands, in turn, to the viscera through its efferent autonomic fibers and also, probably by humoral transmission, stimulates the secretion of the potent pituitary hormones. Neural connections have been demonstrated between the hypothalamus and posterior



Graphic portrayal of neuroendocrine axis as principal mediator between body centers and pathways involved in psychic forces and physiological responses.

pituitary, and a system of blood vessels (the portal system) is present that may convey hypothalamic substances to the anterior pituitary.[8] It is probable that several routes exist whereby the hypothalamus activates the anterior

7. Wolff, H. G.: Protective Reaction Patterns and Disease, Ann. Int. Med. **27**: 944 (Dec.) 1947.
8. Harris, G. W.: The Relationship of the Nervous System to (*a*) Neurohypophysis and (*b*) Adenohypophysis, Proceedings of the Society for Endocrinology, J. Endocrinol. **6**: xvii (Oct.) 1949.

pituitary.[9] The intimate pituitary-adrenocortical relationship, also depicted, requires little comment in this era of corticotropin (ACTH) and cortisone. Long [10] has shown, in addition, that epinephrine from the adrenal medulla, consequent to sympathetic activation, impinges on the hypothalamic-pituitary centers and evokes the increased production of corticotropin and perhaps other pituitary derivatives. There are thus both direct and circuitous routes by which pituitary-adrenocortical function may be stimulated. It is likely that here, as well, additional pathways will be demonstrated.

In brief, these are the mechanisms that maintain our internal economy and mobilize our bodily forces for the fluctuating strains of daily living. With the impact of stress—actual or symbolic, microbe or mother-in-law—psychophysiological responses are called into play by the receptive nervous system and its potent endocrine collaborators. These emergency devices, though vital, are nevertheless costly. They function efficiently for short-term needs alone. When forced to combat prolonged adversity, like a two-edged sword they may so disrupt bodily tissues and processes as to destroy the very organism they were designed to protect.

DIAGNOSTIC CRITERIA

The diagnosis of an emotionally engendered disorder is based on certain definite criteria. All too often this conclusion is achieved by exclusion alone. This is illogical, unnecessary, and frequently dangerous. The basic requirements for a positive "psychosomatic" diagnosis [8] demand that (1) the manifestations of the particular illness, wholly or in part, should be characterized by an onset, sequence, nature, and course that suggest disturbed psychophysiological function. As further corroboration, (2) the physical and laboratory findings should disclose no pertinent structural lesions or, in "mixed" cases, organic disease that explains only partially the total picture. When this is the case, (3) there must then be demonstrated some stressful life situation (or internal conflict) that is currently providing the patient with significant difficulty. Furthermore, (4) the impact of this stress should be correlated, in time, with the onset, exacerbation, or perpetuation of the present illness. To complete the diagnosis, (5) the patient's response to this stressful situation should be related, in significance, with his various symptoms and signs. In other words, his manifestations should reflect, physiologically, his unresolved dilemma or partial though unsatisfactory solution of the problem.

These criteria may appear excessive but are essential, since there is no substitute for a valid diagnosis. In the long run, far more time will be spent unproductively with "functional" patients if these positive criteria are ignored. Sins of omission and commission will be far more likely to occur. Psychogenic illnesses will be mismanaged as serious structural disorders; patients will develop fixed beliefs that they harbor significant organic disease and too easily may be started on the never-ending road of "medical shopping," polypharmacy, polysurgery, and chronic invalidism. Conversely, organic disease, lurking beneath a "functional" exterior or developing in its early stages without physical and laboratory findings, will be easily and frequently overlooked at a time when therapy is still possible. Practitioners must be concerned not merely with the differentiation of psychic disturbances from organic processes but also with the determination of all the factors operating in the patient's disability. Psychic and somatic processes are not mutually exclusive. No one will dispute that even neurotics must die, yet this obvious truism is often forgotten.

THE COMPREHENSIVE APPROACH

The question is frequently raised, particularly by the busy practitioner, "How does one extract the necessary information to satisfy these diagnostic requirements?" I have found quite satisfactory the standard history and physical examination routine, modified elastically to suit the individual patient and bolstered by a few concepts borrowed from our psychiatric colleagues. As emotional disorders are usually reflected in many spheres of activity,[3] important information may be garnered from a survey of the patient's social and vocational history, family relationships, and marital adjustment.

Attitude.—To gain the patient's confidence and elicit this requisite case material, the physician's attitude is all important. His manner should indicate interest and friendly understanding but must avoid overtones of judgment or criticism.

Opening Question.—The history, if not spontaneously initiated by the patient, is best opened by the examiner with some general nondirective question such as "Why have you come to see me?" The patient is then encouraged to discuss his present problems and the factors precipitating his visit. This nondirective approach will occasionally evoke an elaboration of current life difficulties in the light of which the various physical complaints, otherwise disconnected and meaningless, take on significance. It will provide, in any event, a starting point of the patient's choice (which is usually meaningful) from which he may be led into more pertinent areas.

Observant Listening.—For this purpose the art of "observant listening" rather than a barrage of direct and leading questions is of inestimable value. While listening to what the patient says, the doctor observes the way in which it is said. He notes the facial expressions and bodily movements and takes particular heed of those comments that are associated with unusual emotional responses. He takes cognizance of what is inappropriately omitted from the patient's story. Where indicated, of course, simple direct questions are interjected to clarify pertinent points.

"Associative Anamnesis."—The main trend of the discussion, though charted by the patient, is best guided by the examiner into potentially productive channels with the use of a technique called "associative anamnesis." [11] This procedure serves to connect the current complaints with the background on which they occurred and any disturbing factors linked thereto. It consists essentially of rephrasing the patient's own statements in the form of a question so as to initiate further elaboration of some desired topic without injecting any of the examiner's

9. Levine, R., and Goldstein, M. S., in Progress in Neurology and Psychiatry, edited by E. A. Spiegel, New York, Grune & Stratton, Inc., 1951, p. 220.

10. Long, C. N. H.: Conditions Associated with Secretion of Adrenal Cortex, Federation Proc. 6: 461 (May 19) 1947.

11. Deutsch, F.: The Associative Anamnesis, Psychoanalyt. Quart. 8: 354 (July) 1939.

personal concepts. At other times an understanding nod, murmur of encouragement, or quizzical look will suffice to renew the patient's conversational flow should a temporary halt occur. In brief example is the following case:

A young woman with tension headaches of six months' duration casually mentions that these had their onset while she was cleaning house one day shortly after her mother's arrival. As her conversation had momentarily ceased, the examiner inquires, equally casually, "Mother's arrival?" Whereupon (and with an obvious increase in her general tense state) the patient explains that mother is getting on in years, that there is no one else to care for her, and that she is residing with the patient and her husband. After another momentary pause, and aided by an understanding smile from the examiner, the patient blurts out the information that mother, though "ailing" all her life, is far from feeble, is extremely "nervous and fussy," and is living with them much against the husband's wishes. Further encouragement and subtle guidance produces the common story of two women in one home, unexpressed resentment with secondary feeling of guilt on the part of the patient, all intensified by the resultant and concurrent discord with her husband.

Fifteen to 30 minutes of this "observant listening" and "indirect control" at the outset of the history will usually shed much light upon the current illness and, equally importantly, the "person in the patient."

Family History.—Fortified with this information, the examiner can then delve into the patient's family and past histories, at which time additional personal data may be quite easily obtained. While inquiring into the illnesses and deaths of the parents and other key relatives, the examiner should note their dates, the prevailing circumstances, how the patient was involved, and how he reacted. During this phase the patient, if properly stimulated, will also provide material on his wife, in-laws, and children. Thus, his important relationships can be established and some degree of insight gained into the personalities of key individuals. The physician's receptive and noncritical attitude plays the vital role in encouraging the patient to divulge facts and feelings of the past that may have important bearings on the present.

Past Health.—While reviewing the past medical and surgical records, the examiner should attempt to elicit evidence of previous neuropathic traits. Patients will often admit the existence of such patterns in their parents or siblings while unable or unwilling to implicate themselves. This may point toward an unhealthy family environment and/or unstable familial tendencies, in addition to providing information about the patient himself. As any tendency toward emotional instability is more likely to manifest itself during periods of situational stress, certain general, as well as specific, periods demand careful scrutiny. These include early childhood when feeding, bowel, and bladder difficulties appear, the time formal schooling is begun, the age of puberty, the first encounter with the problem of making a living, marriage, the advent of children, the menopause, and such general stresses as illness and death in the family, war, depression, and the like.

Systems Review.—During the systems review, attention is directed toward any adjunctive complaints that commonly reflect disturbed emotional states. Common examples are headaches, syncope, appetite disorders, globus hystericus, pricking precordial pains, certain dyspepsias, bowel dysfunctions, and various menstrual and sexual difficulties. Sleep disorders, unusual dreams, impairment of concentration, and mood alterations are also frequently uncovered at this stage. By the use of subtle indirection, an amazing mass of material may be obtained within the framework of the orthodox medical history and within a relatively short period of time.

Physical Examination.—The physical examination provides the opportunity to detect any objective evidences of emotional dysfunction. Some of the more prominent signs include fluctuating changes in skin color, temperature and moisture, alterations in pupillary size, frequent sighing and other respiratory irregularities, vasomotor lability with fluctuating heart rate and blood pressure, spastic phenomena of smooth and striated muscle, and hyperactive deep tendon reflexes that frequently coexist with a hypoactive or absent gag reflex.[3] Gross inspection will commonly detect general patterns of significance such as excessive anxiety, tension, depression, or an inappropriate pseudo calmness (which has been noted particularly in patients with hysteria, hypertension, and ulcerative colitis [3]).

Final Review.—During or at the completion of the physical examination, the patient will often volunteer valuable information that has thus far been withheld. At this stage also, pertinent questions will be more easily received by the patient, and previous leads may be followed up without undue expenditure of time. The examiner should now be in the position, by virtue of his knowledge of the past history, the patient's characteristic reaction patterns, and the current life situation, to delineate the genesis of the present illness, its underlying purpose, and its more superficial meaning to the patient. It is this fund of knowledge that is so vitally requisite to the planning of subsequent therapy.

PROGNOSTIC AND THERAPEUTIC CRITERIA

The prognostic and therapeutic evaluations, much as the "positive" diagnosis, should be based on definite criteria. Mine are presented herewith. As indicated, (1) the psychic features and (2) any somatic component present are considered in the light of their nature, severity, duration, and significance to the patient. The prognosis of coexistent organic disease is, as far as possible, clearly established. Next, (3) the patient's personality structure and basic emotional stability demand careful analysis. Similarly, (4) the degree of insight present and the patient's motivation to recover are evaluated. In addition, (5) the environmental and interpersonal stresses are assessed to see how, if at all, they may be manipulated. Finally, (6) the patient's age and level of intelligence are considered. Persons in the lower intellectual ranges and those, by virtue of age, without resilience and flexibility are poor therapeutic prospects.

On the basis of these data it shoud be possible to define the patient's needs, assets, and deficits and thus to chart a rational and realistic therapeutic course. The examiner is now in the position to decide which patients require immediate psychiatric referral and which he can handle himself. He is in possession of sufficient information to recognize and accept therapeutic limitations, whether due to psychic or to somatic processes, that have exceeded the reversible range. He has observed more than the duodenum of his patient with peptic ulcer and has

seen beyond the blood pressure of his essentially hypertensive one. Understanding his "patient as a whole," the physician will be able to help him avoid, or better tolerate, those various life stresses that previously have exacerbated these morbid processes. Patients cannot but benefit when their total illness is competently treated.

PSYCHOTHERAPY

Although the scope of this presentation does not permit detailed discussion of psychotherapeutic techniques, some general points will be discussed that, as a nonpsychiatrist, I have found of practical value. The keystone of such therapy is the physician-patient relationship. At the outset it is well to remember that this is not an intellectual exercise wherein the physician imposes his wisdom and wishes on the patient. It is rather to be regarded as a psychological experience during which the patient undergoes emotional readjustment and maturation. In practice, the physician's efforts at understanding the patient's problems are often more important therapeutically than the actual comprehension. Clinicians without formal psychiatric training may thus obtain good therapeutic results without a profound knowledge of psychopathology.

Theoretically, there are two broad forms of psychotherapy: (*a*) expressive or uncovering and (*b*) suppressive or covering. In actual practice there is usually involved an admixture of both. Expressive therapy requires skilled personnel and utilizes specialized methods that are beyond the scope of the average physician. Suppressive therapy, on the other hand, is usually well within the therapeutic domain of the nonpsychiatrist. Although more superficial, this can be very effective. It functions within two main areas: (*a*) the manipulation of the patient and (*b*) the manipulation of the environment. As therapy potentially begins with the initial visit, the physician's warm and interested attitude is the primary important therapeutic step. This will encourage the patient to air his conscious problems, and, if received properly, this will afford him significant relief. Reassurance and encouragement from the understanding physician will provide further support and help allay the patient's anxiety. Superficial insight into the relationship between his emotional problems and physical symptoms with appropriate, simplified explanation of the underlying mechanisms will give the patient additional understanding and frequently dissipate many of his fears. When he appreciates that these disorders are extremely common, that everyone has a tolerance level beyond which he will break, the patient will no longer regard himself as a defective specimen and will tend to regain his self-esteem. In conjunction with these direct efforts it is often necessary to effect certain environmental changes so as to minimize the stressful factors impinging on the patient. For this purpose the relatives or employer should be consulted and their cooperation secured. Similarly, the services of various social agencies should be utilized. Many of these can, and do, render invaluable aid.

To some physicians these therapeutic maneuvers may seem too superficial to be effective. In actual practice the patient's responses testify that deep-seated drives and feelings are being mobilized. These dynamic forces are catalyzed, for good or for evil, by the quality of the physician-patient relationship. Even though the nonpsychiatric therapist may lack full understanding of what is going on, these therapeutic techniques will achieve satisfying and often dramatic results if significant rapport has been developed.

There are certain practical working principles that must be observed when therapy is attempted. The nonpsychiatrist must restrict himself to the discussion of material that is within the patient's awareness. Though he may gain insight into more basic problems, the physician should avoid uncovering forces he cannot control and that may seriously disturb the patient. He must permit the subject to air his fears and feelings rather than "hold the floor" himself. He must avoid premature evaluations and advice lest he destroy the patient's confidence, and, for the same reason, he should not render moral judgments and pointlessly criticize. The physician must not make decisions for the patient; this fosters only further dependency. No patient can be "given" a fresh, mature perspective, but he can be "helped" to achieve it.

SUMMARY

The results of several recent psychomedical surveys are presented. The combined data reveal that psychophysiological disturbances were responsible, wholly or in part, for the illnesses of 949 (47%) of the 2,038 unselected medical patients analyzed. The pertinence of these findings to the general medical population is discussed. Current concepts on the mechanisms underlying these disorders are briefly reviewed. Emphasis is laid on the potential pathological consequences of the conversion of emergency "protective reaction patterns" into chronic states. The neuroendocrine centers and pathways subserving these alterations are delineated.

The basic requirements for a "positive" psychosomatic diagnosis are outlined. These demand a broad evaluation of the present symptoms and signs on their own merit, in the light of the physical and laboratory findings, and as they relate, in time and significance, to current stressful life situations. A comprehensive approach to the patient with "functional" problems is described that is practical and not time consuming, requires no special skills, elicits the usual and necessary medical data and, in addition, provides vital information on the "person in the patient," delineates the related features in the background on which the illness occurred, and renders valuable aid in the planning of therapy.

Criteria are presented on which prognostic and therapeutic evaluations may be based. These necessitate analysis of both the psychic and somatic features of the current illness, the patient's personality structure and emotional stability, his degree of insight and motivation to recover, his external stresses, and his age and intelligence. These data will define the patient's needs, assets, and deficits and will permit rational, realistic therapeutic planning. Psychotherapeutic methods are briefly discussed that are within the province of the nonpsychiatrist. These operate in two main areas: (*a*) the manipulation of the patient and (*b*) the manipulation of the environment. Emphasis has been laid on the keystone of all therapy—"the physician-patient relationship."

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MEDICALLY TREATED SMALL GASTRIC ULCER

FIVE YEAR FOLLOW-UP STUDY OF FOUR HUNDRED FOURTEEN PATIENTS

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For many years at the Mayo Clinic partial gastrectomy has been the treatment of choice in 60 to 70% of cases of apparently benign gastric ulcer.[1] This has been so because the 10% of patients whose ulcers prove cancerous are given the best chances of cure, the morbidity due to benign ulcer is terminated promptly, the results of surgical treatment of the benign ulcer are excellent, and the risk of surgical treatment is small (1 to 2% mortality). In the remaining 30 to 40% of cases medical treatment has been instituted, in some at the insistence of the patient and in others for various reasons with the approval of the physician. In some cases this medical treatment has been instituted at the clinic, but in most cases it has been instituted elsewhere. Such treatment has varied widely in strictness because many physicians with varying viewpoints regarding medical treatment have been responsible.

METHODS OF STUDY

The records of 1,864 patients seen in the years 1940 to 1945 inclusive, in whom the clinical diagnosis of gastric ulcer was made on the basis of clinical and roentgenologic findings, were reviewed. Of these patients, 464 either refused prompt surgical treatment or chose a preliminary period of medical treatment with our consent. Excluded from the study were those cases in which surgical treatment was carried out without initial medical treatment, those in which the gastric ulcer was located in a diaphragmatic hernia, and those in which the diagnosis had been made in previous years. Trial of medical therapy under hospital conditions was instituted at the Mayo Clinic in 153 cases, but no attempt has been made to analyze separately the data from these cases. We simply wished to know what happened to the 464 cases in which medical treatment was begun either here or elsewhere.

Personal interviews, records of return visits and examinations, follow-up letters to patients, follow-up letters to attending physicians, and copies of operative, pathological, and necropsy reports and death certificates were used. Of the 464 patients, 452 (97.4%) were traced. In 38 (8.4%) of the 452 traced patients, we did not obtain information about the results of medical treatment, but we did find that 30 are living and 8 are dead. In the remaining 414 (91.6%) of the traced patients, information about the results of medical treatment was obtained. (In 20 of these, we know only that death was not related to the ulcer.) It is the information obtained in the 414 cases that we shall present.

The sex and age distribution of the 414 patients on whom adequate information about the medical treatment was obtained is given in table 1. The ratio of men to women was about 4:1. The age of the majority of the patients fell within the fourth, fifth, and sixth decades. The sex and age distribution of these patients was similar to that in other series that have been reported.[2]

Of the 414 patients, surgical treatment was urged for and refused by 78. In these cases, medical treatment was instituted against the best judgment of the consultant. In the remaining 336 cases, a preliminary trial of medical treatment was chosen by the patient apparently with the consent of the consultant. The reasons, as nearly as could be ascertained, that consent of the consultant was given are listed in table 2. In most cases it was because the lesion was thought to be benign. In only 31 cases was disease elsewhere in the body given as a reason.

FINDINGS

Results of Medical Treatment.—The results of medical treatment in 414 cases of gastric ulcer clinically diagnosed as benign, in which a preliminary trial of medical treatment was given either on demand of the patient or with consent of the physician, have been summarized in table 3.

If one regards successful medical treatment as meaning complete and permanent healing, then such treatment was possible only in the 85 cases (73 living and 12 dead) in which complete relief was obtained; it was not possible in the 309 cases in which symptoms persisted, and it was uncertain as to results in the 20 cases in which death was caused by conditions unrelated to ulcer. These data mean that, because of the unsuccessful medical therapy, the morbidity of the disease in varying degrees continued in 309 traced patients. It continues in the 130 now living; it continued until death in 39 now dead and until operation was performed in the 140 subsequently operated on. Further details about the 140 surgically treated patients will be given later. Of the 59 deaths, 44 were due to unrelated causes and 15 to related causes; 9 of the 15 were due to gastric cancer. The incidence of gastric cancer in the 189 cases in which surgical treatment was not performed and medical treatment was unsuccessful was 4.8%.

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From the Mayo Foundation, University of Minnesota (Dr. Jordan), and the Division of Medicine (Drs. Cain and Comfort) and the Division of Surgery (Dr. Gray), Mayo Clinic.

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These data permit emphasis on the possibility of the development of gastric cancer late in the life cycle of the stomach diseased with gastric ulcer. Thus, in the 9 cases of gastric cancer occurring among the 274 cases in which only medical therapy was used (3.3%), death resulted from cancer within a year after such treatment was

TABLE 1.—*Sex and Age Distribution in 414 Cases*

Age, Years	Men	Women
10-19	1	0
20-29	4	3
30-39	53	8
40-49	93	19
50-59	108	29
60-69	46	19
70-79	19	8
80-89	2	2
Total	326	88
Percentage	78.7	21.3

started in 3 cases, in four to five years in 1 case, in five to six years in 1 case, in seven to eight years in 3 cases, and in more than nine years in 1 case. It is easy to believe that gastric cancer was already present at the time of the initial examination in the three cases in which death occurred within one year but difficult to believe that cancer already was present in the six cases in which death occurred four to nine years or more later. It may be assumed that in these six cases cancer developed either in the ulcer or in the mucosa surrounding the ulcer. Regardless of the explanation accepted, it seems clear that the physician treating a gastric ulcer medically may not be certain that cancer will not appear sometime later.

It was noted earlier that, of the 414 cases, in 78 surgical treatment was urged but refused and in 336 cases medical treatment was given with the consent of the consultant. It is of interest to compare the results in the two groups. In 9 of the 78 cases (11.6%) the results of medical treatment were satisfactory, in 66 (84.6%) they were unsatisfactory, and in 3 (3.8%) they were un-

TABLE 2.—*Reasons That the Physician Consented to Trial of Medical Treatment in 336 Cases*

Reason	Cases
Cardiac disease	12
Pulmonary disease	6
Old age and senility	5
Tumors elsewhere in body	2 *
Rheumatoid arthritis	1
Alkalosis	1
Cirrhosis	1
Thrombophlebitis	1
Psychoneurosis	1
More urgent surgical measures	1
Ulcer, probably benign	305
Total	336

* Patients lived more than five years.

known. In 10 of the 78 cases (12.8%) the lesion was found to be cancerous. Surgical treatment was employed subsequently in 37 cases (56.1%) of the 66 in which medical treatment was unsatisfactory. Of the 336 cases in which medical treatment was started with the consent of the consultant, such treatment was satisfactory in 76 (22.6%), unsatisfactory in 243 (72.3%), and of unknown results in 17 (5.1%) of cases. In 33 (9.8%) the gastric lesions were found to be cancerous. Of the 243 cases in which the results were unsatisfactory, in 103 (42.4%) surgical treatment was carried out. The success of medical treatment, the percentage of patients who eventually came to operation, and the percentage incidence of cancer are not greatly different in the two groups of cases.

Cases in Which Medical Treatment Was Abandoned and Surgical Treatment Given.—From the study of the 140 cases of gastric ulcer in which medical treatment was abandoned and surgical treatment given, we have obtained data on the duration of medical treatment before surgical treatment, on operative mortality, and on incidence of malignancy. Data on the duration of medical treatment and the reasons for abandoning it are given in table 4.

While failure of the ulcer to heal led to discontinuation of medical treatment in all 140 cases, in 16 the complications of obstruction, hemorrhage, and perforation caused abrupt termination of such treatment. Obstruction and perforation caused termination of medical treatment within a month in two cases each; they also caused termination as long as five years after medical treatment had

TABLE 3.—*Results Observed in Follow-up Study Made Five or More Years After Start of Treatment*

Treatment	Number	Percentage
Medical treatment only		
Complete relief	85	20.5
Partial relief	71	17.2
Unimproved	61	14.7
Worse	37 *	8.9
Uncertain	20 †	4.8
Total	274	66.2
Medical plus surgical treatment	140 ‡	33.8
Total	414	100.0

* Fifteen of the 37 patients died of related causes: 9 of gastric cancer.
† All patients died; deaths not due to related causes.
‡ There were 4 surgical deaths.

been begun. Operative deaths occurred in four cases (2.9%). It will subsequently be noted that three of the four deaths occurred in cases in which cancer was present. In 34 (24.3%) of the 140 cases in which medical treatment was abandoned for surgical treatment, gastric cancer was found. In these cases, the reason for failure of healing is obvious.

Gastric Ulcers Ultimately Proved Malignant at Surgical Exploration.—Analysis of the data from the 34 cases of gastric ulcer ultimately proved malignant at surgical exploration disclosed information about duration of medical treatment and duration of life (The results of surgical treatment in the 106 cases of gastric ulcer of this series proved benign at surgical exploration will be reported at another time.) Information on the duration of medical treatment is summarized in table 5.

Again it may be said that it is not difficult to believe that cancer was present in those cases in which it was demonstrated within one, two, or even three years after the first examination, and that gastric cancer was being treated medically in these instances. It is most difficult to believe, however, that cancer was present at the time of the first examination in those cases in which four, five, or more years intervened between diagnosis and surgical exploration. Regardless of the relationship between ulcer

and cancer, the stomach diseased with gastric ulcer may become the site of cancer three, four, five, six, or even nine years after the demonstration of an intrinsic lesion of the stomach. Of the 34 gastric lesions explored eventually, 9 were found not resectable and 25 were resectable. The hospital mortality rate was 8.8% (three deaths).

The duration of life is known for 31 patients with cancer (table 6). Of the 15 patients who died, in 8 the lesion was not resectable and in 7 it was resectable. Of the eight whose lesions were not resectable all died within the year. Of the seven patients, now dead, whose lesions were found resectable, one survived less than 1 year, one for 1 to 2 years, three for 2 to 3 years, one for 3 to 4 years, and one for 9 to 10 years. Two of these seven patients died of causes other than cancer. Of the 31 patients whose duration of life is known, 12 (38.7%) survived less than one year (3 died postoperatively), 13 (41.9%) lived three years or more, and 7 (22.6%) lived five years or more. That so many lived five years or more after resection is encouraging.

COMMENT

Many pertinent facts about the small ulcerating gastric lesions are known. Some heal spontaneously; others heal rapidly under conditions of good medical management;

TABLE 4.—*Duration of Treatment and Reasons for Abandoning*

Reasons for Operation	Duration, Years: Less Than 1/12	1/12-1	1-5	5 or More	Total
Failure to heal	88	44	35	23	140
Associated conditions					
Obstruction	2	1	2	2	7
Hemorrhage	0	2	3	1	6
Perforation	2	0	1	0	3

still others heal poorly or not at all under the best of conditions. Healing usually means benignancy, but not always, for cancerous ulcers have been known apparently to heal temporarily.[3] Failure of rapid healing to take place does not necessarily mean malignancy. Gastric ulcers tend to recur. About 10% of the small, benign appearing ulcerating gastric lesions are cancerous, and as many as 20 % of those that are operated on have proved malignant.[4] The chances that a gastric ulcer is malignant are greater the larger the lesion (few larger than a dollar are benign [5]), as are the chances of those located on the greater curvature or in the prepyloric region. The same is true of those in older persons, especially when symptoms are of short duration, and of those associated with low gastric acidity. With each recurrence the possibility of cancer recurs, and cancer may appear after many years of medical treatment, as was demonstrated in our group of cases. It is in the variability of the behavior of the gastric ulcer and its response to medical treatment and in the ever-present possibility of malignancy that the problems of treatment of gastric ulcer arise.

The physician wishes to cure by medical means the ulcer that will disappear rapidly and completely. He also desires to avoid prolongation of morbidity if the lesion is benign, or diminution of the chances of surgical cure if it is malignant, by unwise and prolonged medical therapy. Those with wide experience in the field have developed an approach to the problem that tends to achieve these ends.[4b] There is wide agreement that surgical treatment should be given immediately for the perforating, obstructive, or bleeding ulcer, the chronic ulcer with scarring or with an extragastric pocket, the ulcer that is diagnosed as cancer roentgenologically or that presents features

TABLE 5.—*Duration in the Forty-Three Cases in Which Ulcer Eventually Proved to Be Cancerous*

Duration of Medical Treatment, Years	Diagnosis Proved: Surgical Exploration	Clinical Methods or Necropsy	Total
Less than 1/12	10	0	10
1/12-1	7	2	9
1-2	5	0	5
2-3	2	0	2
3-4	3	0	3
4-5	1	2	3
5 or more	6	5	11
Total	34	9	43

making the chances of malignancy great, and those of which careful medical management and long-continued observation will be difficult. Medical management is reserved for those ulcers that are acute, are small, appear to have the least chance of malignancy, and occur in patients who have other disease that increases disproportionately the risk of surgical treatment.

To secure the future cooperation of the patient so as to avoid more than a short period of medical management of the unrecognized cancerous ulcer or prolonged morbidity due to a benign ulcer, it is necessary to discuss with him before medical therapy is started the problems involved and to outline for him the course to be pursued

TABLE 6.—*Known Duration of Life After Surgical Treatment in Twenty-Eight Cases* *

Duration, Years	Dead	Living	Total
Less than 1	9 *	..	9
1-2	1	2	3
2-3	3	..	3
3-4	1 †	3	4
4-5	..	2	2
5-6	..	2	2
6-7	..	..	0
7-8	..	4	4
8-9	..	0	0
9-10	1 ‡	0	1
Total	15 ‡	13	28

* Three immediate postoperative deaths excluded.
† Died of causes unrelated to cancer.
‡ In nine cases lesions not removed when operation was performed.

in his case. The patient is informed that the risk of operation (about 2% mortality if the ulcer is benign) is smaller than the risk of malignancy (about 10%) with

3. Rivers, A. B., and Dry, T. J.: Differentiation of Benign and Malignant Gastric Ulcers: Unreliability of Diagnostic Criteria, Arch. Surg. **30**: 702-715 (April) 1935.

4. (*a*) Welch, C. E., and Allen, A. W.: Gastric Ulcer: Study of the Massachusetts General Hospital Cases During the 10-Year Period 1938-1947, New England J. Med. **240**: 277-283 (Feb. 24) 1949. (*b*) Smith, F. H., and Jordan, S. M.: Gastric Ulcer: Study of 600 Cases, Gastroenterology **11**: 575-593 (Nov.) 1948.

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prolonged medical treatment, and that to give him adequate protection medical management should not be prolonged beyond three weeks unless he becomes symptom free, occult blood disappears from the gastric contents and feces, and the ulcer decreases rapidly in size roentgenologically. The patient also is told that successful management means complete disappearance of the ulcer and permanent healing proved by periodic roentgenologic or gastroscopic examination or both over a period of years, and that surgical treatment will be urged if the ulcer does not heal promptly or if it recurs.

Achievement of such a program of management of the small ulcerating gastric lesion is difficult. It is difficult because clinical and roentgenologic features do not ensure benignancy and do not give a sound basis for choice of therapy. It is difficult (1) because temporary improvement arouses the hopes of the patient that an operation may be avoided, and hence he resists surgical treatment when healing does not take place, (2) because long-continued medical observation and therapy under conditions that protect the patient are difficult, and advice based on honest differences of opinion about choice of treatment varies, and (3) because the physician cannot always provide surgical treatment at a minimal risk. Undoubtedly, the management of gastric ulcer creates a situation requiring a nice choice between the risk of surgical treatment on the one hand and the morbidity of benign ulcer and the risk of cancer on the other.

The results of medical management in our group of cases reflect these difficulties. The results should not be compared with the results obtained in groups of cases [4b] in which treatment is carried out by a small group of physicians under conditions that permit more uniform management and stricter control. In our group of 414 cases the results cannot be called good. Results could not be so designated (1) when complete relief was obtained in only 85 cases, (2) when unsatisfactory relief was obtained in 309 cases (in 140 of which the patients subsequently underwent surgical treatment), (3) when in 15 of the 274 cases in which only medical treatment was used the patients died from related complaints and in 9 of these 15 death resulted from gastric cancer without even an attempt at surgical treatment, (4) when an inoperable cancer was found in 9 cases, and (5) when death in 30 cases may be attributed to the complication of benign ulcer and to cancer. It seems likely that more rigid adherence to the principles of good management than was given in this series and more prompt resort to surgical measures may well have produced better over-all results, reduced the rate of morbidity in many cases, and prolonged life in those cases in which the ulcer was cancerous.

Subsequent diagnosis of cancer in the patient who originally had a benign gastric ulcer needs emphasis. Gastric cancer was diagnosed in this series of cases as long as five years after diagnosis of an intrinsic gastric lesion. Subsequent diagnosis of cancer in this group emphasizes the need for long-continued observation of the patient treated medically for gastric ulcer. The incidence of gastric cancer among benign appearing gastric ulcers deserves comment. The incidence of cancer in the general population is not known with certainty, but it has been estimated [6] at about 1 per 1,000 (about 0.1%) in that portion of the population more than 40 years old (the age group in which 90% occur). The incidence of gastric cancer in the small ulcerating gastric lesion in this and other series is about 10%, or about 100 times as frequent as it is estimated to be in the general population. It also is of interest to compare the incidence of late developing cancers in the patient with benign gastric ulcer with that of the general population. Of our series of 414 patients, 226 were alive and unoperated on five years after medical treatment was started. Eleven gastric cancers developed in these patients, the incidence being 4.9%, which is again many times greater than in the general population. These figures emphasize that gastric ulcer, or the mucosa of the stomach diseased by gastric ulcer, is a precursor of cancer of the stomach.

Cancerous ulcer probably accounts for 5 to 10% of all gastric cancers. It is, therefore, no small part of the general problem of gastric cancer. More important, it is a segment of the general cancer problem in which improvement in successful therapy can be accomplished by wider recognition of the incidence of malignancy among the benign appearing gastric ulcers, avoidance of more than a short period of medical treatment in such cases by more rigid application of the principles of therapy, and more prompt surgical intervention.

SUMMARY AND CONCLUSIONS

A five year follow-up study of 414 benign appearing gastric ulcers, which had been treated medically, was conducted. Medical management proved disappointing. Such treatment was satisfactory in only 20.5% of the cases. Morbidity was allowed to continue even for years in many cases. Medical management was abandoned for surgical treatment in 33.8%.

Cancer was present or developed in 10.4% of the total group. Nine patients died of cancer without an attempt at surgical treatment. Cancer was present in 34 (24.3%) of the 140 patients coming to operation; it was inoperable in 9 of these. Most important, gastric cancer developed in approximately 5% of the patients who had not undergone an operation and who were living at the end of five years. On the other hand it is encouraging that 7 (6 living and 1 dead) of the 34 patients with malignant ulcer survived five or more years after gastric resection.

More rigid application of the principles of good management, it is believed, would have decreased the morbidity, and even have prevented the development, of gastric cancer in patients with gastric ulcer and would have increased the percentage of five year survivals among patients who had cancerous ulcers; however, the difficulties of applying the principles of good medical management and the ensuing unsatisfactory results of medical treatment invite early surgical intervention in a greater percentage of cases than at present.

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6. Discussion on Schiller, W.: Criteria for the Diagnosis of Malignancy in Rectal Polyps, J. Nat. Cancer Inst. 7: 395-424 (April) 1947.

PROCAINE AND PROCAINE AMIDE HYDROCHLORIDE IN SKELETAL PAIN

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Attempts to control the pain of joint disease and its associated syndromes have led to the use of procaine hydrochloride. It has been injected intravenously to relieve the pain of chronic arthritis, especially degenerative arthritis. The relief obtained has not been striking or long lasting. Side-reactions have been common. Better results followed intra-articular injections of this drug.

Procaine hydrochloride injections have not as frequently benefited patients with rheumatoid arthritis. Graubard reported good results with intravenous injections of this agent in rheumatoid arthritis. The claimed effectiveness and harmlessness have been challenged.[1]

Procaine is an ester. It is promptly hydrolyzed by fluids of the human body into its substituent parts: paraaminobenzoic acid and diethylaminoethanol. The splitting of the drug is enzymatic owing to procaine esterase. This esterase is found in plasma, the liver, the lungs, and mucous membranes. The drug cannot be detected in the blood two minutes after the intravenous injection of 150 mg. Spinal fluid has practically no esterase activity.

After 2 gm. of procaine hydrochloride is given orally, none can be detected in the blood. This failure of the orally administered drug to produce a blood level is probably due to the high concentration of procaine esterase in the alimentary mucous membrane.

In spite of the lack of demonstration of the drug in the blood after intravenous administration, important therapeutic effects have followed its injection by this route. Procaine hydrochloride was given intravenously by Bien in 1907. It has been found useful in serum reactions, bronchial asthma, Ménière's syndrome, thromboangiitis obliterans, tetanus, and cardiac arrhythmias, especially those of ventricular type.

Many pains in and about the skeleton and its joints and their attachments are dramatically relievable by regional infiltration with procaine hydrochloride. The necessity for preinjection of barbital and the occasional objectionable and often alarming side-effects restrict the number of patients benefiting from infiltration.

Some patients show a marked idiosyncrasy to procaine hydrochloride. The unfavorable reactions are dermatitis, excitability, nausea, vomiting, tachycardia, falling blood pressure, collapse, convulsions, and even death.[2] Hypersensitivity may be detected by an intradermal injection of 0.1 cc. of 1% procaine hydrochloride. Reactions may be very much reduced in frequency and intensity by administration of enough barbital before injection of the procaine hydrochloride.

PROCAINE AMIDE HYDROCHLORIDE AS AN ANESTHETIC AND ANALGESIC

Procaine amide "pronestyl" hydrochloride differs from procaine hydrochloride only in having an amide linkage instead of an ester linkage. Procaine amide is also hydrolyzed in the human body but far more slowly than procaine. This would suggest that procaine amide would have three advantages over procaine. Its action would be more gradual, more prolonged, and less likely to produce unfavorable reactions. The analgesic properties of procaine, when injected, are well established. Whether injections of procaine amide can produce analgesia has not been investigated. The analgesic effects of an injected drug are not wholly attributable to the chemical. The physical effect of stretching of the nerve endings by the injected fluid is known also to reduce pain in the skin as well as in muscle.

Because of its possible analgesic effect, procaine amide hydrochloride was administered to patients with pains in joints and soft tissues.

ORALLY ADMINISTERED PROCAINE AMIDE HYDROCHLORIDE

After preliminary trials with smaller doses, three 0.25 gm. capsules of procaine amide hydrochloride were given after meals and at bedtime. As no deleterious effects were noted by the patients or found on physical examination, blood cell counts, and electrocardiographic studies, treatment with the drug was continued, 3 gm. daily, for one week or longer. The blood cell counts and electrocardiographs were done routinely at first and occasionally after negative results were obtained. Thirty-two patients with rheumatoid arthritis; 29 with degenerative arthritis; 2 with shoulder-hand syndrome; 1 each with neurodermatitis, dermatomyositis, and ankylosing arthritis of the spine; and 1 with intermittent claudication were so treated.

Five patients with rheumatoid arthritis were symptomatically better, and two claimed to be slightly improved. The sedimentation rates were unaffected. Objectively these few patients were much less stiff and able to perform movements previously impossible. The improvement lasted only as long as they took the procaine amide hydrochloride. They were not as well while taking placebo capsules of the same appearance as the procaine amide. I do not consider that much, if any, importance can be attached to the reported improvement of these patients. Two of the 29 patients with degenerative arthritis claimed to be less stiff while taking 4 gm. of procaine amide hydrochloride daily. The patients with shoulder-hand syndrome, neurodermatitis, dermatomyositis, ankylosing spondylitis, and intermittent claudication were unaffected.

ORALLY ADMINISTERED PROCAINE HYDROCHLORIDE

Procaine hydrochloride was given orally in capsules of 250 mg. each. The usual dose was 3 gm. daily. Of 17 patients with rheumatoid arthritis, 2 professed to have

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From the Arthritis Clinic of Cook County Hospital and the Presbyterian Hospital of Chicago.

Read before the Section on Internal Medicine at the 101st Annual Session of the American Medical Association, June 10, 1952.

Procaine hydrochloride and procaine amide hydrochloride were furnished by Abbott Laboratories, North Chicago, Ill. Procaine amide ("Pronestyl") hydrochloride was supplied by E. R. Squibb & Sons, New York.

1. Keats, A. S.; D'Alessandro, G. L., and Beecher, H. K.: A Controlled Study of Pain Relief by Intravenous Procaine: Report to Council on Pharmacy and Chemistry, J. A. M. A. **147**: 1761 (Dec. 29) 1951.

2. Marton, R.; Spitzer, N., and Steinbrocker, O.: Intravenous Procaine as an Analgesic and Therapeutic Procedure in Painful, Chronic Neuromusculoskeletal Disorders, Anesthesiology **10**: 629 (Sept.) 1949.

in Rectal Polyps, J. Nat. Cancer Inst. 7: 395-424 (April) 1947.

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less pain and stiffness. Objective evidence of improvement or decrease in the sedimentation rate was not observed. Fifteen patients with degenerative arthritis received 3 gm. of procaine hydrochloride daily. Three said their symptoms lessened.

One patient with sciatic pain and degenerative arthritis of the lumbar portion of the spine had less pain while taking procaine hydrochloride in capsules. A patient with radiculitis associated with degenerative arthritis of the cervical part of the spine got no relief from oral use of procaine hydrochloride. One patient each with fibrositis, dermatomyositis, periarthritis of the shoulder, shoulder-hand syndrome, psoriasis, and carcinomatosis had no benefit from procaine hydrochloride given orally. Two 250 mg. capsules of procaine hydrochloride taken after meals controlled perennial endogenous bronchial asthma in one patient and the rash and itching in two patients with exfoliative neurodermatitis.

TABLE 1.—*Results of Oral Administration of Procaine Amide Hydrochloride*

Route	Dose	Duration of Treatment	Disease	No. of Patients	Benefit	Comments
Oral	3 gm. daily	2 weeks	Degenerative arthritis	29	Fewer symptoms in 2	Equivocal to no effect
			Rheumatoid arthritis	32	Fewer symptoms in 7	Equivocal to no effect
			Shoulder-hand syndrome	2	None	No effect
			Ankylosing spondylitis, dermatomyositis, neurodermatitis, intermittent claudication	1 each	None	No effect
Periarticular and intra-articular injection	40 cc. about the joint 15 cc. into the joint	Singly or at intervals	Degenerative arthritis	22	Immediate relief in almost all; gradual recurrence; progressive benefit on repeated injections	Helpful treatment; no advantage of intra-articular over peri-articular injections
			Rheumatoid arthritis	11	Pain on injection; relief of short duration	Not effective treatment
Intravenous	10 cc.	Once	Rheumatoid arthritis	3	None	No effect
			Carcinomatosis	3	None	No effect

TABLE 2.—*Results of Treatment with Procaine Amide Hydrochloride by Injection*

Route	Dose	Duration of Treatment	Disease	No. of Patients	Benefit	Comments
Infiltration	20 to 40 cc.	Single or repeated injections, usually repeated	Perivertebral "fibrositis"; episacral lipomas, "bursitis"—shoulder and hip, periarthritis	44	Prompt, lasting	Preferred treatment
Infiltration of stellate ganglion	10 to 15 cc.	Usually repeated	Shoulder-hand syndrome	15	Prompt; frequently lasting	Satisfactory treatment
Infiltration of brachial plexus	20 to 40 cc.	1 to 4 injections	Shoulder-hand syndrome	12	Prompt, lasted 1 to 4 weeks	Not as effective or lasting as infiltration of stellate ganglion
Radicular	10 cc.	1 to 4 injections	Radiculitis	8	Prompt	Satisfactory treatment

PROCAINE AMIDE HYDROCHLORIDE INJECTIONS

Procaine amide hydrochloride was injected into 118 patients. The pain in three patients with carcinomatosis involving the skeleton was unaffected by 10 cc. (100 mg. per cubic centimeter) injected intravenously. In the remaining 112 patients procaine amide hydrochloride was injected into or about painful areas or into or about nerve roots or the stellate ganglion.

Procaine amide hydrochloride is available as a 10% solution (100 mg. per cubic centimeter). This solution was diluted 10 times for purposes of regional injection, depending on the size of the area to be treated; 10 to 60 cc. (0.1 to 0.6 gm.) was injected at one time into one site.

INTRADERMAL INJECTIONS

Identical areas of the skin in three patients, one with rheumatoid arthritis, one with psoriasis and the mutilating form of rheumatoid arthritis, and one with degenerative arthritis were injected with isotonic sodium chloride solution, with 1% procaine hydrochloride solution, and with 1% procaine amide hydrochloride solution. The degree of analgesia produced and its duration were compared for each injected substance.

No detectable hypesthesia or hypalgesia was obtained by injection of 7 cc. of isotonic sodium chloride solution intradermally. The injection caused severe pain. The injection of 7 cc. of procaine hydrochloride (1%) produced immediate anesthesia to touching with cotton and immediate analgesia to pinprick. The anesthesia and analgesia from this drug lasted one to five hours. After the needle was introduced, the injection caused no further pain.

Intradermal injection of 1% procaine amide hydrochloride solution (7 cc.) caused pain somewhat less severe than was produced by the injection of isotonic sodium chloride solution. For two seconds the pain of injection was as severe as that accompanying injection of sodium chloride solution and then was much less severe than the latter. The injections of procaine amide hydrochloride caused considerably more discomfort than the injection of procaine hydrochloride. Anesthesia to touching with cotton (loss of the epicritic sense) was complete in one to four minutes. Analgesia lasted from one to four hours after the injections of procaine amide hydrochloride were given. One patient said that the skin that had been infiltrated remained numb even 24 hours after the drug was introduced.

INTRA-ARTICULAR INJECTIONS

Fifteen cubic centimeters of the solutions of sodium chloride, procaine hydrochloride, and procaine amide hydrochloride was injected into the synovial cavity of one affected knee of each of the three patients. The joint was entered immediately without infiltration of the overlying skin. The injection of isotonic sodium chloride solution caused severe pain in each patient. However, the arthritic pain was abolished in each instance in 15 to 30 seconds. The relief of the joint pain by the administration of the sodium chloride solution lasted over 24 hours in each of the patients, after which the pain gradually returned and increased over a period of several days. Sensitivity of the skin over the injected joints was unaffected in any instance by the intra-articular saline injection.

Intra-articularly injected procaine amide hydrochloride (1% solution) also relieved the joint pain in 15 to 30 seconds. The joints remained sensitive to touching with cotton. Moderate hypalgesia to pinprick developed.

The experiment on relief of pain obtained by intra-articular injection of procaine amide hydrochloride was also controlled by simultaneous injection of isotonic sodium chloride solution into the opposite joint. Care was taken that the symmetrical joints were equally involved with disease.

A 1% solution of procaine hydrochloride injected into affected knees also relieved the arthritic pain in 15 to 30 seconds. The pain relief lasted over 24 hours. Intra-articular injection of procaine hydrochloride also induced cutaneous analgesia but did not affect sensitivity to pinprick.

There was no appreciable difference in the analgesic effects of intra-articularly administered isotonic sodium chloride solution, procaine amide hydrochloride, and procaine hydrochloride.

PERIARTICULAR AND INTRA-ARTICULAR INJECTIONS

Degenerative Arthritis.—A 1% solution of procaine amide hydrochloride was injected into a knee in 11 patients, a hip in 7 patients, a sacroiliac joint in 3 patients, and a shoulder joint in 1 patient. Because of the relative ineffectiveness of procaine amide as a prompt local anesthetic, 1 to 2 cc. of 1% procaine hydrochloride was regularly used to anesthetize the skin before injection of procaine amide hydrochloride. The pericapsular area of the joint was infiltrated with procaine amide hydrochloride. Immediate relief of pain was the usual experience. Four of the five patients with degenerative arthritis in the knees experienced relief for weeks.

All the patients with degenerative arthritis in the hip noted immediate relief, lasting days to weeks. Injection into the joint, with care not to inject the periarticular tissues, also relieved pain and stiffness. Injection of procaine amide hydrochloride into the joint cavity did not improve the results over those obtained by periarticular infiltration. More than one joint was treated in four patients. The joint and periarticular tissues were treated repeatedly, in some cases as many as six times, at intervals of one to six weeks. Improvement was progressive. The patients had much less pain and stiffness and were able to walk more erectly.

Pain in knees involved by degenerative arthritis was regularly relieved for variable lengths of time by intra-articular injections of isotonic sodium chloride solution, 1% procaine amide, or 1% procaine. The same joints in a given patient at two-week intervals or corresponding joints of a patient were treated with the three solutions in succession. In most, the relief obtained from any of the injected substances lasted about three days, but in many the relief was still appreciable three weeks after a single injection was given. Often the pain would be increased for a few hours by the intra-articular injection of isotonic sodium chloride solution or procaine amide hydrochloride. A lasting decrease of pain would be noticed the day after the intra-articular injection to persist for days or weeks. A difference in the lasting benefit from the sodium chloride solution, procaine amide solution, or procaine solution was not determinable.

The knees of an obese, 50-year-old woman with rheumatoid arthritis were also and predominantly affected by degenerative changes. The knees in this patient were markedly benefited by an intra-articular injection of 1% procaine amide hydrochloride.

Rheumatoid Arthritis.—Ten cubic centimeters of the 10% solution of procaine amide was given intravenously to three patients with rheumatoid arthritis without any benefit. Six patients with rheumatoid arthritis were given injections about an involved knee with procaine amide hydrochloride. One ankle in a patient with rheumatoid arthritis was similarly infiltrated. The average amount used was 40 cc. of a 1% solution. Immediate but transient relief resulted in all cases. Injection of the joint cavity itself did not improve the results obtained by periarticular injection.

Intra-articular injections given in knees involved by rheumatoid arthritis in four patients successively, at weekly intervals, with isotonic sodium chloride solution, 1% procaine amide, and 1% procaine did not result in any relief. Injection into and about joints involved by rheumatoid arthritis gave relief for days and even weeks, but the relief obtained was decidedly of shorter duration than that secured by similar injections in patients with degenerative arthritis. Injection into joints affected by rheumatoid arthritis occasioned much more pain than did injection of the joints of patients with degenerative arthritis.

Radiculitis.—Infiltration with procaine amide hydrochloride of the nerve roots in patients with radiculitis due to pressure from protruding intervertebral disk, to osteophytes in degenerative arthritis of the spine, or to postherpetic neuralgia always gave immediate relief from pain. Two of the eight patients treated for root pain were still relieved two months after a single injection. The remaining six patients required repeated injections, some as many as six times, before lasting, marked relief was obtained. Injecting 40 cc. of a 1% solution of procaine amide into the epidural space immediately relieved lumbar root pains causing sciatica and presumably due to protruding intervertebral disks.

Fibrositis.—In four patients, painful lumps (fibrositic episacral nodules), with sciatic radiation of pain in two, were injected with 3 to 5 cc. of procaine amide, with immediate relief in all. In two patients it was necessary to inject the nodules twice, the pain having slightly recurred after two weeks.

A large number of patients with pain of the lumbago type in the low back muscles were regularly relieved by injection of procaine amide hydrochloride into spots of maximum tenderness. In cases of a few days' duration, one injection sufficed.

Painful conditions about the shoulder, excluding arthritis of the shoulder and its associated joints and also excluding the shoulder-hand syndrome, are variously recognized as periarthritis, tendinitis, and bursitis. The results of injection of procaine amide hydrochloride about the shoulder, into its associated bursae, and about its tendons were highly satisfactory. Relief of pain was marked, prompt, and lasting in various degrees. Pain on injection was slightly greater than that experienced on injection of procaine hydrochloride. In patients with recent symptoms the area had to be treated two to three times. Patients with a history of pain and stiffness for months were given injections as many as 12 or more times. The injections were followed by active exercise.

The left fourth costosternal articulation was infiltrated, with prompt and lasting relief, in a patient concerned about "heart pain." Two other patients with painful tender spots in the intercostal spaces anterior to the heart, feared by the patients as due to heart disease, were relieved of the pain by one to three injections of 3 to 5 cc. of procaine amide hydrochloride into the skin and muscle in the precordial area. The painful area of the lumbar portion of the spine was successfully infiltrated in a patient with the "facet syndrome."

Shoulder-Hand Syndrome.—It is usual to produce a Horner's syndrome by infiltrating the region of a stellate ganglion with procaine hydrochloride. This syndrome, indicating paralysis of the cervical sympathetic area, usually develops within a few minutes after an adequate injection of procaine hydrochloride anterior to the seventh cervical tubercle. A Horner's syndrome was never obtained by injection of 10 cc. of 1% procaine amide hydrochloride about the stellate ganglion in 15 patients. Notwithstanding this, the symptoms and findings of the shoulder-hand syndrome were relieved by a stellate ganglion injection of procaine amide hydrochloride in 15 patients presenting the shoulder-hand syndrome. The benefit was immediate and observable for days to weeks after the injection.

Injection of the three cords of the brachial plexus with 20 to 40 cc. of procaine amide hydrochloride gave prompt and lasting benefit in 12 patients with shoulder-hand syndrome. Presumably, the benefit was the result of the procaine paralysis of sympathetic fibers in the plexus.

SIDE-EFFECTS

Ventricular extrasystoles disappeared from a patient after 20 cc. of 1% procaine amide hydrochloride had been injected into painful nodules in the region of the sacroiliac joints. A Negro girl, 20 years old, had rheumatoid arthritis. On receiving 5 cc. of a proposed 20 cc. of the drug about an involved wrist, she experienced an epileptiform attack. According to her history she had had several spontaneous epileptic convulsions over a period of years. Three possible explanations of the attack in our clinic exist. Administration of the drug may have lowered her convulsive threshold, permitting an attack to occur. The fear, excitement, and pain of the injection may have provoked an attack. The attack may have been a coincidence. Considering the properties of procaine, the attack was likely a result of injection (psychic and physical trauma) of a convulsant into a patient with idiopathic epilepsy.

None of the patients receiving injections experienced giddiness, nausea, or tachycardia.

Earlier, the injections of procaine amide hydrochloride were preceded by an oral dose of pentobarbital sodium, 1½ to 3 grains (0.096 to 0.128 gm.). In later treatments pentobarbital sodium was given only to the most apprehensive patients.

Three of the patients taking procaine amide orally complained of inappetence and slight nausea with a dose of 2 gm. daily. Two patients receiving the same dose complained of slight giddiness. Three of the patients receiving 3 gm. of procaine hydrochloride daily complained of giddiness.

The electrocardiogram, blood cell count, and sedimentation rate were unaffected in several patients so tested. Studies of six patients with normal hearts showed no cardiovascular effect of much larger doses of procaine amide hydrochloride than those used in this study (up to 1 gm.). The blood pressure, pulse rate, and electrocardiogram were unchanged. The patients with various types of organic heart disease, except sinus mechanisms, were also tested with intramuscular doses of procaine amide hydrochloride, without any discoverable change in their cardiovascular findings.

COMMENT

Procaine amide hydrochloride is much less effective as a quick-acting local anesthetic than is procaine hydrochloride. The chief advantage of the former over the latter is the relative absence of objectionable side-effects, rendering less necessary with procaine amide hydrochloride injections the precautions usually demanded on injection of a similar amount of procaine hydrochloride. When given orally in large daily doses, procaine amide hydrochloride does not relieve pain. In similar doses, oral use of procaine hydrochloride seemed to relieve the pain in a few patients with rheumatoid arthritis. Oral administration of procaine hydrochloride controlled two instances of hypersensitivity: bronchial asthma and neurodermatitis. Procaine amide hydrochloride, injected intravenously, did not relieve the pain of carcinomatosis or rheumatoid arthritis.

CONCLUSIONS

Procaine amide hydrochloride given orally is ineffective as an analgesic. Oral administration of procaine hydrochloride controlled severe bronchial asthma in one case and severe exfoliative neurodermatitis and rheumatoid arthritis in another case.

Procaine amide hydrochloride produces hypesthesia and analgesia when injected into the skin. It relieves the pain of fibrositis, radiculitis, and degenerative arthritis, often for considerable periods, when injected into painful soft tissues, about nerve roots, and into and about joints.

Isotonic sodium chloride solution, 1% procaine amide hydrochloride in isotonic sodium chloride solution, and 1% procaine hydrochloride in isotonic sodium chloride

solution are about equally effective in relieving the pain of degenerative arthritis when injected into the synovial cavity. These solutions do not similarly relieve the pain of rheumatoid arthritis when injected intra-articularly. Undesirable side-effects were fewer with injections of procaine amide hydrochloride than with equivalent amounts of procaine hydrochloride. Because of a decreased incidence of unfavorable reactions, procaine amide hydrochloride solutions are preferable to procaine hydrochloride for infiltration to relieve pain in cases of degenerative arthritis, "fibrositis" (including periarthritis and bursitis), pain of radicular origin, and the shoulder-hand syndrome.

122 S. Michigan Ave. (3).

CLINICAL NOTES

SYNDROME OF RUPTURED DEEP EPIGASTRIC VESSEL

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The clinical picture of bleeding into the rectus abdominis muscle, though infrequent, is important in the differential diagnosis of acute intra-abdominal catastrophe. The conditions simulated may be legion, and the correct diagnosis depends primarily on the examiner's awareness of this disease. Recent observation of two cases, the condition in one simulating twisted ovarian cyst and in the other ruptured diverticulitis, has emphasized the necessity of knowledge of this condition.

The classical concept of the syndrome of ruptured deep epigastric vessel is that of the sudden or insidious development of a tender palpable mass, usually in the lower part of the abdomen, initiated by trauma, as in cough, and occurring most frequently in the aged, obese, or debilitated. Strain, acute or chronic, initiates the vessel rupture. The severity of the attendant trauma, and the anatomic limitations [1] determine the extent of hemorrhage and the subsequent signs and symptoms. These are often devious and have been described in detail by Kapsinow [2] and others. Primary disease states [3] are frequently present; among these, tetanus, typhus, and miliary tuberculosis have been noted. In one case the condition complicated whooping cough. Age, obesity, pregnancy, and blood vessel atheroma favor the development of vessel rupture.

The symptom complex is marked by severe, often agonizing, abdominal pain, occasionally accompanied by a shock-like state. Slight fever or subnormal temperature and leukocytosis or a normal white blood cell count, depending on the rapidity, amount, and duration of bleeding, may be present.

Diagnostic needle aspiration is usually futile, since the hemorrhage is interspersed among the muscle fibers. Laffont's sign (ecchymosis around the umbilicus, in a slowly developing hemorrhage) or Fothergill's sign (a fixed palpable mass that is still present when the patient sits up) are helpful in differential diagnosis.[4] As a rule, however, the chief aid in diagnosis is an awareness of the disease.

REPORT OF CASES

CASE 1.—The patient, a 45-year-old white woman with compensated rheumatic heart disease (mitral insufficiency, mitral stenosis) was seen at home, complaining of sudden nausea and excruciating pain in the right lower abdominal quadrant. The onset followed a spell of coughing and was accompanied by increased sweating and restlessness, the patient rolling on the floor in agony. Examination was difficult because of extreme tenderness, but a 10 by 4 cm. mass in the right lower abdominal quadrant, extending to the inguinal canal, was palpated.

The last menstrual period had occurred two weeks previously. The patient had had a low grade fever and cough of two days' duration. The temperature was 100.4 F (rectal), pulse rate 90, and blood pressure 170/80. The hemoglobin was 13.3 gm. and white blood cell count 4,500, with 34% segmented and 38% nonsegmented polymorphonuclear cells, 22% lymphocytes, and 6% monocytes. The urine was normal.

Examination with the patient sedated revealed a markedly tender mass in the right lower abdominal quadrant, with the dimensions previously mentioned, and an otherwise soft, nontender abdomen. The preoperative diagnosis was twisted ovarian cyst or Richter's hernia. At surgery extravasation of blood throughout the lower half of the right rectus muscle was found. No abnormal changes in the peritoneal cavity were demonstrated.

CASE 2.—A 34-year-old white man had a history of chronic glomerulonephritis and duodenal ulcer, which had healed. His initial complaint was moderate tenderness in the left lower abdominal quadrant, first noted two days after he had moved heavy furniture. The onset was insidious, with gradually increasing tenderness. There were no accompanying gastrointestinal or genitourinary symptoms. Examination revealed a sausage-shaped mass, 8 by 4 cm. in the left lower abdominal quadrant, pointing toward the inguinal canal. The mass was exquisitely tender and accompanied by muscle guarding. There was positive rebound tenderness. Rectal examination revealed brown feces but no masses or tenderness.

Subsequent studies revealed a temperature of 99.2 F (oral), pulse rate 80, and blood pressure 160/110. The white blood cell count was normal. Urinalysis indicated albuminuria (4+) and 3 to 5 red blood cells, 8 to 10 white blood cells, and 3 to 4 hyaline casts per high power field. A fixed localized mass was felt in the prone and upright positions in the left lower abdominal quadrant, and a healed McBurney incision on the right was noted. Barium enema revealed spasm of the lower sigmoid. Aspiration of the superficial mass with a 15 gage needle was unproductive.

A diagnosis of ruptured inferior epigastric vessel was made and conservative treatment adopted. Within one week the tender mass had subsided, and results of another barium enema were normal. Follow-up examination two weeks later revealed complete disappearance of the mass and absence of tenderness.

COMMENT

The picture in these cases conforms in general to that of epigastric vessel rupture. The patients were slightly younger than is usual, but during World War II rectus muscle rupture with hematoma was observed in young parachutists.[5] Both patients had chronic disease states,

1. Cullen, T. S.: Lesions of the Rectus Abdominis Muscle Simulating an Acute Intra-Abdominal Condition: Hemorrhage into or Beneath Rectus Muscle Simulating Acute Abdominal Condition, Bull. Johns Hopkins Hosp. **61**: 317 (Nov.) 1937.

2. Kapsinow, R.: Rupture of the Deep Epigastric Artery, New Orleans M. & S. J. **98**: 507 (May) 1946.

3. Robertson, H. M.: Haematoma of Abdominal Wall (with Rupture of the Rectus Abdominis Muscle) Simulating Intra-Abdominal Tumor, Canad. M. A. J. **36**: 606 (June) 1937.

4. Herrman, C.: Rupture of the Deep Epigastric Vessels, Am. J. Surg. **71**: 553 (April) 1946.

5. Mailer, R.: Spontaneous Haematoma of the Abdominal Wall, Brit. M. J. **1**: 637, 1936.

though neither revealed any outward indication of poor vessel structure. The initial trauma in one resulted from cough and in the other from moving furniture. The clinical signs and symptoms and eventual course were typical.

The chief aids in diagnosis are history, the appearance of a fixed palpable mass, and an alertness to this syndrome. In severe and moderate bleeding, surgery is usually necessary. The mild condition may be treated conservatively. Concomitant pathological changes must be corrected.

SUMMARY

The signs and symptoms of deep epigastric vessel rupture are briefly reviewed. A report of two cases is included.

116 Petersville Rd.

USE OF ESTROGEN CREAMS

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and
Franklin I. Harris, M.D., San Francisco

Any woman may go to the drug counter today and purchase cosmetic creams and lotions containing estrogenic substances of varying composition and concentration without a prescription. When the agents of the Federal Food and Drug Bureau first approached physicians for some guidance as to policy in this matter, the consensus was, despite warnings that had appeared in THE JOURNAL,[1] that the total amount of estrogenic substances that would be absorbed by inunction in the amount and concentration recommended would not be likely to produce constitutional effects. We were among those who held this view. The fallacy of this belief is illustrated in the following case.

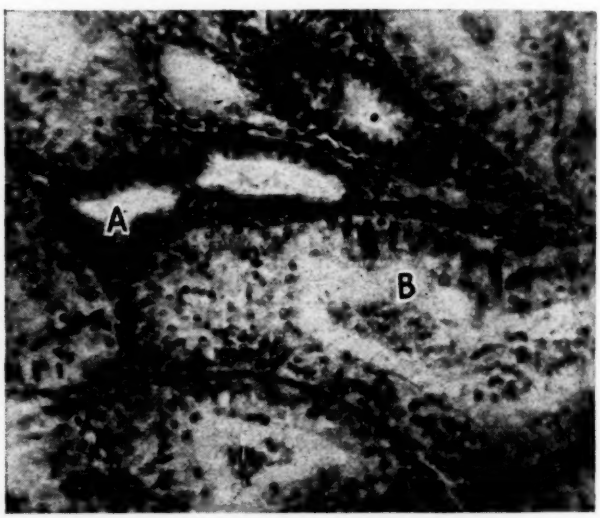
REPORT OF A CASE

Mrs. F. B., aged 40, had lost both of her ovaries by the age of 29 as a result of two tubal pregnancies. In June, 1943, she was referred to one of us (M. B. G.) for weight reduction and treatment of her menopausal symptoms. Flushes, sweats, nervousness, irritability, and insomnia disappeared completely with the oral administration of 1 mg. of diethylstilbestrol daily for 25 consecutive days each month, and withdrawal bleeding occurred regularly according to plan. This type of cyclic control was maintained satisfactorily for five years. Between August, 1948, and February, 1949, the patient failed to return for follow-up. When she did return she complained bitterly of severe "crushing" headaches; she had had one episode of irregular vaginal bleeding and was observed to have palmar erythema. Diethylstilbestrol therapy was discontinued, and vitamin B complex and crude liver were administered parenterally. The prompt return of severe menopausal symptoms necessitated the resumption of estrogen therapy. At first estradiol dipropionate was given parenterally, but in May, 1949, oral treatment with ethinyl estradiol was substituted.

The patient was not seen again for two and a half years. In October, 1951, she came to one of us (F. I. H.) with the following story: She had stopped taking estrogens early in 1950 and had had no bleeding for seven or eight months. Neither did she have more than a minimum of flushes or sweats. In December, 1950, she had taken a "few" diethylstilbestrol pills and had "a normal menstrual period." In September, 1951, after she had taken 1 mg. of diethylstilbestrol, vaginal bleeding again occurred. This bleeding, which began Sept. 20, continued without cessation through Oct. 31. Diagnostic curettage on Nov. 1 yielded considerable grayish hyperplastic endometrium. Microscopically, atypical hyperplasia of the endometrium was demonstrated. There was no evidence of cancer (see the accompanying figure).

Uterine bleeding from a hyperplastic endometrium in the absence of functioning ovaries or of estrogen administration seemed incredible. There could be only two possible explanations: (1) either some ovarian tissue remained from the first operation for ruptured tubal pregnancy (severe hemorrhage at the second precluded satisfactory exploration) or (2) the patient was not telling the truth when she categorically denied taking more than a total of 3 or 4 mg. of diethylstilbestrol during the entire preceding two years.

It was felt that exploratory laparotomy was in order and that, since the uterus in this case was a potential source of danger and fulfilled no useful purpose, a hysterectomy should be performed. On Jan. 17, 1952, at laparotomy, no ovarian tissue was found. The uterus measured 8.5 by 5 by 4 cm. The myometrium was thick, firm, and pale and measured 2 cm. at the widest point. On microscopic examination, focal adenomyosis and myometrial fibrosis was seen. The endometrium was thin and dark and showed only proliferative glands.



There are closely packed irregular endometrial glands (*A*), many of which show marked piling up of stratified hyperplastic epithelial cells. (*B*). There is no evidence of cancer.

There was still no explanation for the abnormal bleeding from a hyperplastic endometrium in the absence of ovarian stimulation until it was ascertained that since August, 1948, the patient had been using unusually liberal quantities of cream and lotion containing estrogens. The label on the 4 oz. (120 cc.) jar stated that the cream contained 10,000 I.U. of natural mixed estrogens per ounce, and that on the lotion, 7,500 I.U. per ounce. The patient had been using each month a 4 oz. jar of the cream, which she liberally applied to face, neck, arms, and legs in addition to small but unknown amounts of the lotion. Therefore she was using by inunction approximately the equivalent of 10,000 I.U. of estrone per week. The freedom from flushes and sweats could thus be explained, as well as the interference with the artificial menstrual cycles, which had been so regular before the use of the cream was begun. When she discontinued use of the hormone cream, flushes and sweats returned. These have since been controlled by oral use of estrogen.

COMMENT

The cyclic use of estrogens in dosages sufficient to produce regular endometrial shedding according to plan offers no therapeutic problems, especially when pelvic organs and breasts are examined regularly. It is only the

From the Division of Medicine and the Division of Surgery, Mount Zion Hospital.

1. Endocreme—A Cosmetic with a Menace, editorial, J. A. M. A. **110**: 1194 (April 9) 1938; The Public be Warned, editorial, ibid. **114**: 1886 (May 11) 1940.

haphazard use or the continuous administration of estrogens that leads to difficulties. In our patient a satisfactory response to cyclic use of estrogens had been maintained for five years, until, without our knowledge, she unwittingly began continuous use of additional estrogens by inunction. During the two years when inunction was the sole method of administration, she had only a minimum number of flushes and sweats, but the continuous absorption of relatively small doses produced insidiously a pronounced degree of endometrial hyperplasia. When bleeding did commence from this hyperplastic endometrium, it was prolonged and heavy.

CONCLUSIONS

The following conclusions may be drawn from the foregoing report:

1. Continuous absorption of small doses of estrogens over a long period of time can produce endometrial hyperplasia.

2. Physicians should be aware of this extraneous source of estrogens and should remember to ask about the use of hormonal creams.

3. If estrogen creams continue to be sold over the counter without prescription, it should be mandatory that the label bear a warning advising intermittent and not continuous use as well as a statement recommending a limitation of quantity to be used.

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CANCER OF THE PROSTATE IN INFANTS AND CHILDREN

Matthew H. Griswold, M.D., Dr.P.H., Hartford, Conn.

The average age at the time of admission to Connecticut hospitals of patients with malignant tumors of the prostate is about 70 years. Sarcoma of the prostate seems to be rare [1] and can occur at any age, although there is evidence that it has a predilection for the younger age groups, about 25% occurring within the first decade.[2] True cancer of the prostate, carcinoma, is seldom seen in infants and children, but other forms of malignant tumors may develop.[3]

REPORT OF CASES

CASE 1.—On July 22, 1944, a 2-year-old infant was admitted to a Connecticut hospital because of complete retention of urine. The history indicated that one month prior to admission the child suddenly began to complain of burning and frequency of urination. No previous history of urinary disturbance could be obtained. The child had learned to control his bladder. At that time the family physician was consulted, and sulfathiazole was prescribed for a period of two weeks and then stopped because urination was becoming less frequent. A specialist was consulted, and the child was admitted to a hospital. Upon physical examination the bladder was found to be palpable above the symphysis before evacuation, and after evacuation there was still a large mass, about the size of an orange, to be felt in the same region. Rectal examination revealed a round mass involving the prostate and extending upward above the examining finger. This mass was elastic to the feel, not fluctuating, not irregular, and not nodular. On July 27, the tumor was removed. Microscopic examination of the surgical specimen showed a rhabdomyosarcoma grade 3 of the prostate with invasion of blood vessels. The patient died on Sept. 6, 1944, and postmortem examination confirmed the diagnosis, demonstrating a recurrent tumor at the primary site, fixed to adjacent tissues and involving the wall of the rectum.

CASE 2.—A second case of malignant tumor of the prostate in the very young was reported by another Connecticut hospital, the date of admission being Sept. 19, 1949. This patient, a 6-year-old boy, had complained two days prior to admission of urinary disturbance and frequency and backache on the right side. Upon physical examination the bladder was found to be distended up to the level of the umbilicus and the prostate was very firm and nodular, similar to that of a cancerous gland in an elderly man. A punch biopsy of the prostate and a biopsy of the inguinal lymph nodes were taken and upon microscopic examination reported by the pathologist as anaplastic malignant tumor grade 3. Suprapubic drainage was instituted on Oct. 11, 1949, and radon seeds implanted in the prostate. The patient was discharged and readmitted two weeks later when the prostate was found to be three times larger than normal and stony hard. Early in March, 1950, arrangements were made for this child to be admitted to the Children's Hospital in Boston. At that institution physical examination revealed a large prostate, which seemed to contain a few hard nodules, and generalized lymphadenopathy. The pathological slides that came with the patient were reviewed by the pathology department at Children's Hospital who diagnosed it as "undifferentiated malignant tumor unclassified." On March 4, 1950, a sternal biopsy showed invasion of the bone marrow with malignant cells, type undetermined. There were numerous metastases throughout the left lung and metastases in the bodies of vertebrae D6, L3, and L5. The patient died on March 25, 1950, the final diagnosis being "possible neuroblastoma."

COMMENT

There have been 2,532 cases of prostatic malignancy reported to the Connecticut Cancer Record Register in the period 1935-1949. Only these two cases were in children, which illustrates the rarity of this condition in the lower age groups. Neither of these cases of malignant disease of the prostate in young persons was carcinoma. The first was a rhabdomyosarcoma and the second an undifferentiated unclassified malignant tumor, possibly a neuroblastoma. Such cases in children appear universally to carry a poor prognosis [4] and present many difficulties in diagnosis and management.

165 Capitol Ave.

1. Foucar, F. A.: Rhabdomyosarcoma of the Prostate in a Child, Am. J. Path. **11**: 753, 1935.
2. Katzan, P.; Cohen, H., and Steiner, M. M.: Rhabdomyosarcoma of the Prostate, Am. J. Dis. Child. **56**: 321, 1938.
3. Ewing, J.: Neoplastic Diseases: Treatise on Tumors, ed. 4, Philadelphia, W. B. Saunders Company, 1940, pp. 851-853.
4. Katzan, Cohen, and Steiner.[2] Greig, D. M.: A Case of Rhabdo-Myosarcoma of the Prostate in a Child Aged 4 Years, Brit. J. Child. Dis. **5**: 185-189, 1908.

Manual Removal of Placenta.—Manual removal of the placenta is an operative procedure which carries with it a higher incidence of hemorrhage and morbidity than spontaneous expulsion of the placenta, and cannot be considered a preferable procedure. Any factor causing excessive bleeding in the third stage or which tends to cause prolonged uterine contraction will tend to increase the incidence of manual removal. Manipulation of the fundus prior to expulsion of the placenta and general anesthesia are factors in excessive bleeding. The use of oxytocics prior to completion of the third stage decreases bleeding, but increases the incidence of incarceration of the placenta. Manual removal of the placenta is indicated without delay in the event of bleeding during the third stage, or after retention for a period of time in the absence of bleeding. Manual removal of the adherent placenta after proper preparation is preferable to violent fundal manipulation in attempts to express the placenta from the uterus. With judicious management, prompt blood replacement and prophylactic antimicrobial agents, manual removal of the placenta can be performed with a minimum of hazard and subsequent morbidity.—H. Halsey II, M.D., Manual Removal of the Placenta, *American Journal of Obstetrics and Gynecology*, July, 1952.

CONGENITAL HEART BLOCK

REPORT OF A CASE

Michael Bernreiter, M.D.
and
Frank O'Connell, M.D., Kansas City, Mo.

Heart block, an interesting and rare complication, is almost always associated with interventricular septal defect. Congenital heart block without evidence of a septal defect was found in two siblings, in one of whose parents there was also a Wolff-Parkinson-White syndrome.[1] Histological studies reported by Yater [2] disclosed a separation of the auriculoventricular node from the bundle of His by a central fibrous body. Other rare causes of heart block are bacterial endocarditis with inflammatory changes to the septum, neoplasm, tuberculosis, and cysts invading the conducting tissues. Aneurysm of the sinus of Valsalva has also been noted in congenital heart block.[3]

In itself congenital heart block is not serious and is apparently compatible with a long life and full activity. The serious prognosis in some cases is determined by associated cardiac anomalies. In the series of 44 cases collected by Yater [4] and co-workers, symptoms were uncommon and cyanosis was absent in 24 and slight or occasional in 14.

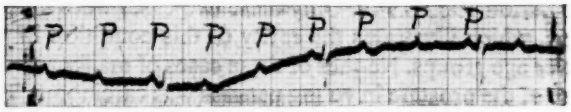

Fig. 1.—Electrocardiogram obtained on the day of birth, showing a 3: 1 auriculoventricular block. The auricular rate was regular and 165 per minute; the ventricular rate was regular and 55 per minute.

REPORT OF A CASE

A baby girl was born Jan. 2, 1951, in St. Mary's Hospital. The attending physician had noticed fetal bradycardia before birth and a pulse rate of approximately 55 per minute after delivery. An electrocardiogram was taken three hours after birth (fig. 1). There is a 3:1 auriculoventricular block. The auricular rate is approximately 165 per minute and the ventricular rate 55 per minute. A loud systolic murmur was best heard along the left sternal border. The murmur did not extend to the cervical vessels. A systolic thrill could not be felt. There was mild cyanosis on crying only. The diagnosis was congenital heart block associated most likely with a defect of the membranous portions of the interventricular septum.

The infant made fairly good progress during the next two weeks. On the 14th day after birth a second electrocardiogram was taken (fig. 2). The auriculoventricular block, although still present, had changed from a 3:1 to 2:1. The auricular rate was now 175 and the ventricular rate 87 per minute. The baby left the hospital in apparently good condition and was not seen again till she was 14 months old, when the mother finally brought her to the office after many invitations by phone and mail. The baby had progressed fairly satisfactorily, but the weight gain was slightly below normal. An electrocardiogram (fig. 3) obtained at that time showed an irregular auriculoventricular block, alternating from 2:1 to 3:1. The auricular rate was regular at 166 per minute, and the ventricular rate varied between 77 and 60 per minute.

On March 28, 1952, about 10 days after the last electrocardiogram (fig. 3) was taken, the patient entered the Children's Mercy Hospital with the chief complaint of swollen face and extremities. Moist and dry rales were heard in all lung fields; the heart was

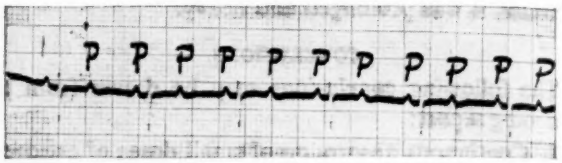

Fig. 2.—Electrocardiogram obtained on the 14th day after birth. There was a 2: 1 auriculoventricular block. The auricular rate was regular and 175 per minute; the ventricular rate was regular and 87 per minute.

enlarged to the left and revealed a machinery-like murmur; the abdomen was greatly enlarged; the liver extended five fingerbreadths and the spleen two fingerbreadths below the costal margin. There was a daily elevation of temperature to between 100.4 F (38.0 C) and 102.2 F (39.0 C). On April 2, at 8:30 a. m., the child died of apparent heart failure.

Postmortem findings showed the heart to be moderately enlarged. A 15 mm. defect in the membranous portion of the ventricular septum was found. The aorta was displaced to the right, riding partially over the defect in the ventricular septum. The pulmonary valve showed thickening of the valve cusps, and the commissures were grown together slightly. Other findings were chronic passive congestion of the liver and the spleen, pulmonary congestion, and focal atelectasis.

In most cases of congenital heart block there is found, as in this baby, a defect of the membranous portion of the interventricular septum. The irregularity of the auriculoventricular block demonstrated in our case is of special interest. The septal defect results from failure of the bulbar septum to close completely the interventricular foramen. This defect is often combined with dextraposition of the aorta and stenosis of the pulmonary artery (tetralogy of Fallot).

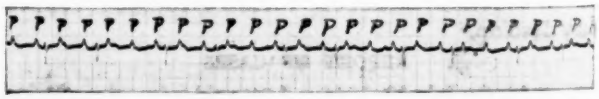

Fig. 3.—Electrocardiogram obtained at 14 months of age. There was an irregular auriculoventricular block alternating between 2: 1 and 3: 1. The PR interval varied between 0.26 and 0.16 second. The auricular rate was regular and 166 per minute; the ventricular rate varied between 77 and 60 per minute.

SUMMARY

A case of irregular congenital heart block associated with septal defect and representing the syndrome of tetralogy of Fallot is reported. A 3:1 auriculoventricular block was demonstrated on the day of birth, which changed to a 2:1 auriculoventricular block 14 days later. When the baby was 14 months old the auriculoventricular block was alternating between 2:1 and 3:1. The child died 10 days after the last electrocardiographic tracing was taken. The findings at autopsy are reported.

432-436 Professional Bldg. (Dr. Bernreiter).

From the Department of Cardiology, St. Mary's Hospital.

Drs. Nicholas Jaime and George Kealhofer of Kansas City referred this case to us for electrocardiographic study. Dr. Richard C. Schaffer reported the findings at autopsy.

1. Wendkos, M. H., and Study, R. S.: Familial Congenital Complete A-V Heart Block, Am. Heart J. **34**: 138, 1947.

2. Yater, W. M.: Congenital Heart Block: Review of Literature: Report of Case with Incomplete Heterotaxy: Electrocardiogram in Dextrocardia, Am. J. Dis. Child. **38**: 112, 1929.

3. Duras, P. F.: Heart Block with Aneurysm of Aortic Sinus, Brit. Heart J. **6**: 61, 1944.

4. Yater, W. M.; Lyon, J. A., and McNabb, P. E.: Congenital Heart Block: Review and Report of Second Case of Complete Heart Block Studied by Serial Sections Through Conduction System, J. A. M. A. **100**: 1831 (June 10) 1933.

SPECIAL ARTICLE

This is the third of a series of articles on cancer. The first article appeared in THE JOURNAL *Oct. 11 (page 587) and the second Oct. 18 (page 688).*—ED.

EARLY DIAGNOSIS OF CANCER OF THE LUNG

Louis H. Clerf, M.D.
and
Peter A. Herbut, M.D., Philadelphia

Tremendous strides have been made in the surgical treatment of bronchogenic carcinoma since the first successful pneumonectomy by Graham in 1933. In reviewing the surgical literature, however, the reader is impressed by the fact that successful surgical treatment can be accomplished only if carcinoma is recognized early. Advanced carcinoma still remains the hopeless problem it always has been. Additional progress will be made only when carcinoma is suspected early and appropriate diagnostic procedures are instituted promptly so that the disease may be treated without unnecessary delay.

Bronchogenic carcinoma has steadily increased in incidence until it is now the commonest form of cancer. During 1948, deaths in the United States from bronchogenic carcinoma alone exceeded 16,000. It is important, therefore, that a lively interest be manifested in this disease, that all physicians become "cancer of the bronchus-minded," and that all diagnostic aids be utilized whenever necessary. Since some of these aids are not generally available or cannot be used in every patient with symptoms referable to the respiratory tract, a practical approach to diagnosis must be found that is available to the general practitioner in his routine office studies.

The results of a number of mass chest surveys show that many carcinomas thus discovered were asymptomatic, that practically all those explored were resectible, and that a majority showed no lymphatic spread. It is obvious that this method of detection would be ideal, but unfortunately it would necessitate two or three roentgen studies annually of the chest of every male adult between the ages of 40 and 70, in which group lung cancer has its greatest incidence. Until such time that adequate detection facilities are available and the laity have been impressed with their importance, reliance must be placed on the general practitioner, the chest physician, and the internist to diagnose promptly the symptoms of the patients who consult them.

SYMPTOMS

Bronchogenic carcinoma presents no characteristic clinical picture. In the early stages the disease may be asymptomatic and is ushered in with an acute episode that is frequently diagnosed as viral pneumonia. Too often the onset is so insidious that it may not be suspected by either the patient or his physician; in fact, it may not be suspected until the case is hopeless. Cancer of the lung is frequently confused with other less serious pulmonary lesions and quite properly has been designated as a masquerading disease. Often, plans of therapy are instituted before adequate examinations are made, and in this way valuable time is lost needlessly. It is important, therefore, in the diagnosis of bronchopulmonary disease occurring in a male adult, to recognize that while certain groups of symptoms and physical signs may mean certain clinical entities, an early restudy and reevaluation of the case is imperative if therapeutic responses are not prompt and if improvement is not continuous. In the symptomatic patient a careful history and physical examination are necessary. Often a careful inquiry into symptoms may suggest carcinoma or at least the need for further investigation.

The commonest first symptom of bronchogenic carcinoma and the one most commonly noted in all reported series of cases is cough. Unfortunately, a majority of patients with carcinoma are smokers, notably of cigarettes, and practically all such smokers have cough (particularly in the morning) with some expectoration. It is therefore difficult to differentiate between a smoker's cough and the cough of carcinoma. In general, it may be said that the cough of carcinoma is not limited entirely to the morning, is of an irritative character, may be troublesome at night, and is often nonproductive of sputum. When making inquiry into symptoms, particularly cough, it is important to ascertain if there has been any change in its frequency or character.

In early cases of bronchogenic carcinoma, sputum is scant. It may occasionally be blood tinged but commonly is mucoid. Hemoptysis, whether slight or of considerable quantity, should never be disregarded; and when it occurs in a male adult it should always be thoroughly investigated by every diagnostic measure available. It is reported as occurring in 55 to 60% of all patients with bronchogenic carcinoma. Pain is usually not an early symptom; instead, there is a sensation of consciousness of one's chest and a feeling of discomfort (not painful) that is comparatively common and should always be regarded with suspicion. Pain simulating pleurisy is not commonly observed in early carcinoma.

Dyspnea or shortness of breath is observed in approximately one-half of the patients with lung cancer. It cannot be explained on the basis of loss of function of a considerable portion of lung tissue, since it may be observed in patients who have relatively early lesions. Wheezing respiration, a symptom frequently overlooked because it is usually observed only in the early stages of the disease, is most important. Any adult patient who has wheezing (commonly observed on expiration) that may be heard more loudly on one side of the chest than the other generally has partial bronchial obstruction. While this symptom is not specifically diagnostic of carcinoma, since it can also be produced by a clump of secretion, its persistence warrants further investigation. Symptoms such as hoarseness, weakness, and weight loss are not of themselves of any significance in detecting lung cancer; however, their presence should merit further investigation, particularly when they are observed in conjunction with the symptoms discussed above.

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DIAGNOSTIC PROCEDURES

Physical Examination.—Since a physical examination often reveals remarkably little information, it should not necessarily be concluded that there is no bronchopulmonary disease simply because there is an absence of definite physical signs.

Roentgen Examination.—Every patient who has one or more of the above noted symptoms that cannot be explained satisfactorily should have a roentgen study of the chest, for this is unquestionably the most important single diagnostic aid in determining the presence of bronchogenic carcinoma. Positive roentgen findings are important. In a majority of the series of cases reported, some change was observed on the roentgen films in from 95 to 98% of all patients checked. While no positive diagnosis of carcinoma could be made in all instances, the presence of demonstrable changes warranted further studies. The physician should not be satisfied with a single roentgenogram of the chest or with a fluoroscopic examination only. Full use of other views should be made in every questionable case that shows any abnormal shadow whatsoever, and, in certain instances, a bronchographic study may be carried out by the radiologist if he believes this will aid in establishing a diagnosis. An objection to the use of iodized oil in the latter study may be raised in that it tends to add additional shadows that may be confusing.

In every case where there is a suspicious lesion on a roentgen film, a definite diagnosis should be made as promptly as possible. Too often shadows are interpreted as viral pneumonia, unresolved pneumonia, pneumonitis, tuberculosis, or other conditions. While not every patient with a lesion in the chest has carcinoma, it is imperative that a positive diagnosis be established or that carcinoma at least be ruled out. With this in mind, further investigations should be promptly carried out. The custom of making roentgenograms at stated intervals of many weeks or months is time consuming and, in the case of carcinoma, invariably allows a lesion to become inoperable. The physician should never delay more than a week or 10 days at the most for comparative roentgen studies. If tuberculosis is suspected, sputum studies, gastric washings, and possibly guinea pig inoculations or the culture of material for tubercle bacilli can be utilized. Here again, however, the physician must act promptly, for in the case of carcinoma the period of operability is very brief.

Bronchoscopy.—The next procedure of great importance in suspected bronchogenic carcinoma is bronchoscopy. The examination encompasses (1) visualization of the tumor within a bronchus or of alterations in the bronchial tree, (2) biopsy of tumor, and (3) collection of secretions for cytological study. Information thus obtained is extremely useful and, in certain clinics, has contributed enormously to the early diagnosis of carcinoma. Direct visualization and biopsy of the tumor are possible only in growths occurring in the larger bronchi. Such lesions are often advanced. While tumors in the peripheral bronchi or "around the corner" in the upper lobes are not often visualized, cytological studies have been extremely helpful in determining their presence.

Cytological Examination.—This procedure in the diagnosis of carcinoma of the lung has come to the foreground only in recent years, although the idea back of it is almost 100 years old. The materials available for study consist of (1) sputum, (2) spontaneously discharged bronchial secretions, and (3) bronchial washings. Details regarding cytological techniques have been published and reviewed previously.[1] In this presentation only the methods of collection and the preparation of the material to the point where it reaches the cytologist will be briefly outlined.

Cytological examination of expectorated sputum is the easiest from both the general practitioner's and the patient's standpoints. Unfortunately, it is not as fruitful as examination of bronchoscopically removed secretions. In sputum collection, the patient should be instructed to first cleanse his mouth and pharynx and then expectorate from "the depths of his lungs" into a suitable, preferably wide-mouthed, glass jar. Either material expectorated at a single sitting or that collected over a 12 to 24 hour period is satisfactory for examination. Sputum that reaches the cytologist within an hour or two after expectoration needs no preservative, while that with an unavoidable delay en route should be fixed in about four times its amount of 95% ethyl alcohol. From the cytologist's point of view, it is preferable to receive sputum material soon after expectoration. If this is impossible or if the material is to be sent by mail, we have found that preparation of smears at the source is more desirable than preliminary fixation in alcohol. The procedure is quite simple. After the sputum has been collected, it should be spread out in a Petri dish over a black background. Bloody areas or gray particles should be fished out and transferred to three new clean glass slides, each of which is then covered with a separate slide. By compressing and pulling the pairs of slides back and forth, the material is spread uniformly over the inside surfaces in a thin film. Next, the slides are pulled apart and immediately fixed in equal parts of 95% alcohol and ether for 10 minutes. After this, they may be removed, allowed to dry at room temperature, and be stained in an appropriate manner at any desired time.

Cytological examination of bronchoscopically removed secretions is unfortunately more difficult than cytological examination of sputum, for, in addition to the inconvenience to the patient, the former process also requires the services of an expert bronchologist. The procedure, however, is more than compensated for by the higher incidence of positive diagnoses. If secretions only are desired, they may be collected during an ordinary bronchoscopic examination from the bronchus that drains the suspected tumor area, either after by-passing the secretions in the trachea and other bronchi or after aspirating them in a separate collector. While the ordinary collector may be used, its excessive tubing is undesirable and it is better to employ a special collector attached directly to the aspirator. If bronchial washings

1. Herbut, P. A., and Clerf, L. H.: Bronchogenic Carcinoma: Diagnosis by Cytologic Study of Bronchoscopically Removed Secretions, J. A. M. A. **130**:1006-1012 (April 13) 1946. Herbut, P. A., and Clerf, L. H.: Cancer Cells in Bronchial Secretions, M. Clin. North America **30**:1384-1392 (Nov.) 1946. Clerf, L. H., and Herbut, P. A.: Primary Carcinoma of the Lung: The Role of Bronchoscopy in Diagnosis and Treatment, New York State J. Med. **49**:907-909 (April 15) 1949. Clerf, L. H.; Herbut, P. A., and Nealon, T. F., Jr.: Cytologic Studies and Prognostic Results in Bronchogenic Carcinoma, Ann. Otol., Rhin. & Laryng. **60**: 840-846 (Sept.) 1951.

are to be obtained, the general procedure is similar to that outlined above, except that the bronchus draining the suspected tumor site is washed gingerly with a sodium chloride solution, after which the washings are aspirated. In either procedure, the collected material is treated exactly the same as is sputum.

Results of Cytological Examination.—Most reports in the literature record positive diagnosis of bronchogenic carcinoma by cytological examination of sputum in from 40 to 65% of all cases. Because the primary purpose of cytological examination is to make the diagnosis early, we have stubbornly adhered to the examination of bronchial washings and have been gratified at our rather consistent results. In a series of 540 consecutive patients with carcinoma of the lung, we have been able to make a positive cytological diagnosis in 476, or 88.3%. In the same series, a bronchoscopic biopsy was positive for carcinoma in 167 patients, or 30.9%. There was, in addition, indirect bronchoscopic evidence of tumor in such forms as bronchial stenosis and fixation in 180 patients. Bronchoscopy was completely negative for tumor and neoplastic cells were found in 156 patients, or 28.8%.

SUMMARY

The two most important items in the early diagnosis of carcinoma of the lung are a high index of suspicion and the determination to carry out the various diagnostic procedures without delay. From a clinical viewpoint, the following factors should be considered: cough, expectoration, pain, discomfort, dyspnea, wheezing respiration, abnormal pulmonary shadows in roentgenograms, and bronchoscopy. From a pathological viewpoint, a bronchial biopsy and the cytological examination of sputum, bronchial secretions, or bronchial washings are mandatory. A positive preoperative morphological diagnosis (biopsy or cytological examination) is desirable in all cases; but if such diagnosis cannot be obtained and if the possibility of carcinoma cannot be ruled out clinically, an exploratory thoracotomy is indicated.

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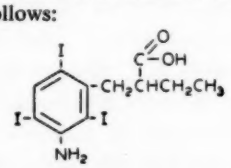
NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

R. T. STORMONT, M.D., *Secretary.*

Iodopanoic Acid.—Telepaque (Winthrop-Stearns).—$C_{11}H_{12}I_2NO_2$.—M.W. 570.97.—β-(3-Amino-2,4,6-triiodophenyl)-α-ethylpropionic acid.—The structural formula of iodopanoic acid may be represented as follows:



Actions and Uses.—Iodopanoic acid is a water-insoluble organic iodine compound administered orally as a radiopaque medium in cholecystography. Following ingestion it is promptly absorbed, eliminated in the bile, and subsequently stored in the gallbladder. It produces dense shadows of the gallbladder usually with a single average dose, which often permits visualization of the extrahepatic ducts.

Iodopanoic acid seldom produces undesirable reactions and has a low toxicity. Occasionally, nausea and diarrhea and, rarely, dysuria have followed its administration. It is contraindicated in acute nephritis and uremia and should not be administered when disorders of the gastrointestinal tract prevent absorption of the compound.

Dosage.—The usual dose is 3 gm. administered orally 10 hours prior to the time scheduled for roentgenography. In addition, the patient should be given a fat-free meal the evening before medication and allowed nothing by mouth until roentgenograms have been taken. The patient should also be given a saline or sodium bicarbonate enema shortly before roentgenography to remove any accumulated gas; immediately following roentgenography, a high-fat meal is given. Additional films are obtained one to three hours later to determine the contractile function of the gallbladder. Visualization of the extrahepatic ducts can usually be obtained if roentgenograms are taken 10 minutes after the high-fat meal. When these structures are of particular interest, the dose of iodopanoic acid may be increased to 5 or 6 gm.

Tests and Standards.—

Physical Properties: Iodopanoic acid is a cream-colored, tasteless powder with a faintly aromatic odor, m.p. 152-158°, which darkens on exposure to light. It is soluble in acetone, alcohol, and dilute alkalis; and insoluble in water.

Identity Tests: A 0.00075% alcoholic solution of iodopanoic acid, prepared as directed in the spectrophotometric assay, exhibits ultraviolet absorption maxima at about 230 mμ [specific absorbancy, E(1%, 1 cm.), about 667] and at about 315 mμ.

Purity Tests: Suspend about 1 gm. of iodopanoic acid in 50 ml. of water, mix well, and filter. To the filtrate add 1 ml. of silver nitrate T.S.: no more than a trace of opalescence appears (*absence of appreciable amounts of iodide*).

Dry about 1 gm. of iodopanoic acid at 105° for 30 min.: the loss in weight does not exceed 1.0%.

Char about 0.1 gm. of iodopanoic acid, accurately weighed, over a low flame, cool the residue, add 1 ml. of sulfuric acid, heat cautiously until evolution of sulfur trioxide ceases, ignite, cool and weigh: the residue does not exceed 0.1%.

Assay: (Iodopanoic Acid) Prepare a 0.00075% solution of iodopanoic acid as follows. Transfer to a 100 ml. volumetric flask 75 mg. of iodopanoic acid, accurately weighed, and dissolve it in a little alcohol. Fill to the mark with alcohol and mix. Transfer to a second 100 ml. volumetric flask 10 ml. of this solution, fill to the mark with alcohol, and mix. Finally transfer to a 100 ml. volumetric flask 10 ml. of this last solution, fill to the mark with alcohol, and mix. Spectrophotometrically determine the absorbancy in a 1 cm. quartz cell at 230 mμ, using alcohol as a blank. The concentration of iodopanoic acid in the solution in mg./ml. = absorbancy ÷ 66.7. The amount of iodopanoic acid present is not less than 95.0 nor more than 105.0%.

(Iodine) Transfer to a nickel crucible about 0.5 gm. of iodopanoic acid, accurately weighed, and add a mixture of 4.5 gm. of sodium hydroxide and 0.5 gm. of potassium nitrate. Heat the crucible gently at first, then more vigorously, for 30 min. after the melt clears. Cool, transfer the crucible to a beaker, add 100 ml. of water, and heat on a steam bath to dissolve the material. Wash the crucible with small portions of water and add the rinsings to the beaker. Acidify with nitric acid, and add exactly 35 ml. of 0.1 *N* silver nitrate and 2 ml. of ferric ammonium sulfate T.S. Titrate the excess silver nitrate with 0.1 *N* potassium thiocyanate. Each milliliter of 0.1 *N* silver nitrate consumed is equivalent to 0.01269 gm. of iodine and 0.01903 gm. of iodopanoic acid. The amount of iodine is not less than 64.0 nor more than 69.4%, equivalent to not less than 96.0 nor more than 104.0% of iodopanoic acid.

Dosage Forms of Iodopanoic Acid

TABLETS. *Assay:* (Iodopanoic Acid) Weigh 20 tablets and powder them. Transfer to a 100 ml. volumetric flask an amount of the powder, accurately weighed, equivalent to about 75 mg. of iodopanoic acid. Add about 75 ml. of alcohol and shake for 1 hour. Fill to the mark with alcohol, mix well, and filter, discarding the first 50 ml. of filtrate. Transfer to a second 100 ml. volumetric flask 10 ml. of the filtrate, fill to the mark with alcohol, and mix. Finally transfer to a 100 ml. volumetric flask 10 ml. of this last solution, fill to the mark with alcohol, and mix. Spectrophotometrically determine the absorbancy in a 1 cm. quartz cell at 230 mμ. The concentration of iodopanoic acid in the solution in mg./ml. = absorbancy ÷ 66.7. The amount of iodopanoic acid is not less than 95.0 nor more than 105.0% of the labeled amount.

(Iodine) Weigh 20 tablets and powder them. Transfer to a nickel crucible an amount of powder, accurately weighed, equivalent to about 0.5 gm. of iodopanoic acid. Proceed as directed in the assay for iodine in the monograph for Iodopanoic Acid starting with, ". . . and add a mixture of 4.5 gm. of sodium hydroxide. . . ." Each milliliter of 0.1 *N* silver nitrate consumed is equivalent to 0.01903 gm. of iodopanoic acid. The amount of iodopanoic acid is not less than 95.0 nor more than 105.0% of the labeled amount.

Winthrop-Stearns, Inc., New York.

Tablets Telepaque: 0.5 gm. U. S. Trademark 610,113.

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GAMMA GLOBULIN AS A PROPHYLACTIC IN POLIOMYELITIS

In this issue of THE JOURNAL appear three articles concerning the use of gamma globulin as a prophylactic agent in the paralytic form of poliomyelitis. The preliminary report of the results is encouraging. It indicates that in the dose employed Red Cross gamma globulin provided significant protection against paralytic poliomyelitis for the observation period of at least five weeks. A final evaluation of the trials will come only after many more months of clinical observation and careful laboratory and statistical analysis to determine duration of immunity, antibody titer required to achieve an immune status, and the effect of gamma globulin in permitting or preventing inapparent infections that would affect the patient's ability to develop an active, long-lasting protection against future exposures.

It is of importance that Red Cross gamma globulin collected from pools of thousands of blood donors in different geographical areas was used in the trials. Such material had been found by Bodian to contain considerable amounts of neutralizing antibodies to all three types of poliomyelitis virus in about equal amounts. Whether commercially available gamma globulin contains similar amounts is yet to be determined.

This demonstration of the usefulness of gamma globulin in poliomyelitis poses a serious problem of materially increasing the available supply of the blood fraction. The need of children in this field should strengthen the understanding of the American people concerning the usefulness of blood and its products and the need for amassing large volumes of blood. If one considers the eager participation of the public in the gamma globulin field trials it is safe to assume an equally enthusiastic response in any future project designed to increase the supply of the blood fraction. At present, the placental source of gamma globulin has not been fully utilized.

Obviously, the attention of many physicians will be focused on that brief section of the articles listing the numbers of poliomyelitis cases that occurred in the control group as compared with those in the group who received injections of gamma globulin. It is recommended, however, that a careful reading be made of the large section of the report dealing with the planning and conduct of the human field trials, for it is also in the philosophy of the experiment and not solely in the results that the true significance of these human field trials can be found.

The concept of strict neural invasion of poliomyelitis virus had become established as a baseline for most experiments in animals in which poliomyelitis is not a natural disease. The field trials reported in this issue of THE JOURNAL, together with the previous demonstration by Enders, Weller, and Robbins [1] that poliomyelitis virus can be grown on extraneural tissue cultures, help greatly the development of a new perspective concerning the natural human disease that much of the animal work has failed to reveal.

The 55,000 children who participated in this research problem are dynamic proof of the confidence of the American people in our system of medicine and medical research. Drawn from all walks of life and from a variety of communities, these children and their parents represent a cross section of public reaction to American medicine. The public participated voluntarily, first as contributors of dimes and dollars to the National Foundation for Infantile Paralysis, which financed the tests, and as contributors of their blood, then as participants in the field studies. Throughout every step of the trials voluntary cooperation was conspicuous. Organized medicine and public health agencies endorsed the project and through their participation contributed immeasurably to its accomplishment.

A striking feature of the study was the explanation of a scientific test to large numbers of the public, through which their cooperation and participation was enlisted. This demonstrates the high degree of scientific understanding of the American people.

ANTICIPATION IN INHERITANCE OF DIABETES

Anticipation, or antedating, is a term applied to the phenomenon of the onset of a hereditary disease at a progressively earlier age in successive generations of an affected family. Woodyatt and Spetz [1] investigated the onset of the disease in the offspring of diabetic parents in 100 families, in each of which the disease has been known to occur in members of two or more generations. Anticipation was noted in 90 of these 100 families. The advance proceeded at the rates of 20 and 34 years per generation. In the eight families in which the disease occurred in three successive generations there were instances in which anticipation was not exhibited in the second generation but was exhibited in the third. In all the families that showed the trend in two successive generations the average difference between the age of onset in the two generations was 20 years. In all families in

1. Enders, J. F.; Weller, T. H., and Robbins, F. C.: Cultivation of the Lansing Strain of Poliomyelitis Virus in Cultures of Various Human Embryonic Tissues, Science **109**: 85 (Jan. 28) 1949.

1. Woodyatt, R. T., and Spetz, M.: Anticipation in the Inheritance of Diabetes, J. A. M. A. **120**: 602-605 (Oct. 24) 1942.

which the disease skipped a generation, the average difference was 45 years, or 22½ years per generation. The whole course of the disease could be run in two generations, but is more commonly completed in three or four, and rarely in more; that is to say, one rarely finds a family with a history of diabetes in more than four generations. Woodyatt and Spetz [1] stressed the practical application of their findings in relation to the estimation of probability that the disease will appear in as yet unaffected relatives of diabetic patients. They believed that anticipation results from progressive degeneration of the germ plasm.

Steinberg and Wilder [2] share the view of most geneticists and do not ascribe any biological significance to the phenomenon of anticipation. They believe it to be statistical rather than a biological phenomenon. They call attention to the following sources of error in the collection of family histories of diabetic patients: 1. Until the introduction of insulin in 1922, many persons with early onset of diabetes did not live to become parents. 2. Despite the introduction of insulin, diabetic women, until very recently, produced relatively few viable offspring. 3. Family histories collected at clinics where diabetes or its symptoms are the reason for the patient's attendance tend to be those of patients with relatively severe diabetes and therefore of patients with earlier ages of onset than the average. Clinical experience indicates that in a majority of the cases in which a parent and a child are diabetic the age at onset in the child is lower than in the parent. In 67.5% of the 251 cases in their series the onset of diabetes was in an earlier decade in the patient than in the diabetic parent.

Utilizing the material of Joslin and his associates,[3] comprising 12,740 cases, these authors demonstrate that calculations based on these figures would predict on the average that 64.3% of all family histories collected from the families in which diabetes occurred in two successive generations would be expected to show anticipation.

A possible biological rationale for anticipation could be looked for when the patient's mother is diabetic. It is well established that many infants born of prediabetic and diabetic women show characteristic abnormalities. It might, then, be assumed that this unfavorable uterine environment causes earlier onset of diabetes among the offspring in whom the disease will subsequently develop. This, however, does not apply when the patient's father is the affected parent, because children of diabetic fathers do not have these disabilities. The frequency of anticipation in cases in which the affected parent became diabetic before the age of 50 is 43.3% when the mother is the affected parent and 42.9% when the father is the diabetic parent. It appears, therefore, that the unfavorable uterine environment provided the fetus by the diabetic or prediabetic mother is not the major factor in determining the age of onset of diabetes in their diabetic offspring.

Steinberg and Wilder [2] stress the variability in age of onset as sufficient in itself to lead to a high frequency of earlier age of onset of a disease in the affected children of affected parents, even when there is no relation between the age of onset in parent and child. The magnitude and frequency of the effect would depend on how variable the age of the onset of the disease is and on how much of the reproduction period is included in this interval. Factors such as increased mortality rate, lowered fertility in a portion of the parental generation or earlier detection in the second generation, either because of prior knowledge of the occurrence of disease in the family or of improved medical techniques, or bias in selecting cases, would tend to enhance

VOTE NOVEMBER 4

Nov. 4, 1952, is a day of great importance to the American people. Americans are the freest people on earth. They live in the most outstanding republic the world has ever seen. Recently, however, Americans have lost some of their freedom by exchanging their personal liberties for government subsidies. There has been a trend in recent years for the executive branch of our federal government to usurp the authority of the legislative branch. This trend, if continued, will lead to totalitarianism.

Democracy works only when all the people take part in it. When only 51% of the electorate exercise their right of franchise, as was the case in 1948, we are governed by 26% of the population. That means we are no longer a democracy but an oligarchy.

Centuries ago Plato said, "The penalty that good men pay for refusing to take part in government is to live under the government of bad men."

All professional groups have a bad voting record. Only a minority have been good citizens in this respect. If the American way of life is to continue, then this record must change. While physicians must be scientists, they must be citizens first, and they must accept not only the privileges but also the responsibilities of citizenship.

The American Medical Association is not a political organization. It can support neither a party nor a candidate. As an organization devoted to public service, it can, however, urge all its members to vote and urge them to see that the members of their families and their friends vote. They have no more important duty in the days immediately ahead. How they vote is between themselves and their consciences. If they do not vote they are not good citizens.

Only by universal participation in our elections can true American democracy be maintained and protected from un-American ideologies. VOTE!

LOUIS H. BAUER, M.D., President
American Medical Association.

2. Steinberg, A. G., and Wilder, R. M.: An Analysis of the Phenomenon of "Anticipation" in Diabetes Mellitus, Ann. Int. Med. **36**: 1285-1296 (May) 1952.

3. Joslin, E. P.; Root, H. F.; White, P.; Marble, A., and Bailey, C. C.: The Treatment of Diabetes Mellitus, ed., 8, Philadelphia, Lea & Febiger, 1946.

the observed differences. This explanation is probably applicable to many if not all reported instances of anticipation in disease with variable age of onset. It certainly appears to be the explanation in the case of diabetes.

Harris,[4] in his study of 1,241 diabetic propositi, felt that there was little or no parent-child correlation with respect to age in onset of the disease. Steinberg and Wilder [2] feel that, because anticipation in diabetes is a statistical and not a physiological phenomenon, it would be desirable to discontinue the use of the term "anticipation" in referring to cases of prior onset of the disease in children of affected parents. The more noncommittal and more descriptive expression "prior onset," they feel, is to be preferred.

The prior onset of diabetes in the diabetic child of diabetic parents is observed frequently because the age of onset of diabetes is highly variable and includes the reproductive period and nearly all diabetic patients who become parents become diabetic after the age of 30 years. There is no biological relation between the age of onset in the parent and in the child. The age of onset of diabetes in a parent cannot be used to predict the age of onset in the children.

INDUSTRIAL NOISE AND IMPAIRED HEARING

Although noise has long been tolerated in industry as a necessary evil, a growing awareness of its manifold implications has been expressed recently in medical, industrial, legal, and labor circles. The fact that noisy industrial surroundings reduce efficiency has received little attention, even though it has been demonstrated that noise reduction pays substantial dividends in terms of higher output, fewer mistakes, and improved morale among employees. Actually, noise costs money, because authentic claims for hearing loss due to industrial noise are often compensable.

As commonly encountered in daily life, noise represents unwanted sound. Exposure to noise for long periods frequently results in loss of hearing among employees. In industry, noise occurs at various intensities and frequencies, but no satisfactory correlation of intensity and frequency has been established as the borderline of safety. Intensity and duration of noise are of prime importance, for the louder the noise the greater the hearing impairment, and the longer the duration of exposure to noise the greater the loss of hearing.

Prolonged exposure to damaging noise levels produces a temporary, physiological loss of hearing, which is recoverable after a period of rest; however, if exposure continues, the ensuing hearing loss grows, with subsequent recovery incomplete. In early cases of noise deafness, the audiometer records a characteristic dip at or near the 4,096 frequency cycle. Early loss may increase further to involve frequencies in the speech range, and when this occurs, the hearing loss soon becomes apparent to the employee. Generally, the evolution of impaired hearing is slow and insidious and the average employee is likely to either disregard it or be unaware of its existence until he is quite deaf.

Various factors influence the degree of hearing impairment following prolonged exposure to hazardous noise. The more important of these are intensity of noise, duration of exposure to noise, frequency spectrum of noise, age of the employee, coexisting ear disease, character of the environment in which noise is produced, distance from the source of noise, position of each ear with respect to sound waves, and individual susceptibility to noise. Use of the last factor has been made in preemployment audiometric tests.

Claims for damage due to impaired hearing have been made through common law actions on the basis of alleged negligence. In this connection, Symons [1] points out that hearing loss due to noise should be differentiated from many other causes of nerve impairment. Considerable controversy centers about acceptable procedures for determining the percentage loss of hearing. Unfortunately, there is discrepancy in the various methods extant, as well as difference of opinion as to whether any method that utilizes only the pure tone audiometric record renders an accurate picture of the ability to understand the spoken voice. More complicated, perhaps, than these issues are claims for impaired hearing that have been entered in law courts through workmen's compensation procedure. Such claims have posed entirely new concepts of workmen's compensation awards, especially since no loss of earnings has resulted from hearing loss.

In view of the inability of medical and surgical therapy to restore permanent hearing loss due to noise, a cardinal objective at present is to institute protective measures in industry and to conserve the hearing of employees and others engaged in activities on the industrial scene. In order to achieve this goal, the cooperation of employees, industrial management, the medical profession, safety engineers, physicists, and union officials, to mention an important few, is required. Several major spheres of investigation and methodology for the control of industrial noise have been proposed, as, for example, (1) surveys of noisy industrial areas; (2) preemployment audiometric and otologic studies of employees; (3) audiometric studies of employees exposed to hazardous noise; (4) the establishment of quantitative standards for evaluating hearing loss; (5) use of preemployment selectivity tests to discover noise-susceptible persons; and (6) the development of procedures to reduce or eliminate noise, by redesigning machines and tools, by creating noiseless industrial processes, or by the use of ear plugs and ear defenders.

According to Fox,[2] there is still some unawareness of the noise problem. However, when interested groups are educated to the need for careful investigation of the traumatic noise hazard at its source of origin, there is a strong likelihood that measures will eventually be discovered to control and prevent hearing loss. In this connection, the example of past cooperative efforts of industry and labor to eliminate other occupational hazards offers adequate hope for the successful solution of the industrial noise problem.

4. Harris, H.: Familial Distribution of Diabetes Mellitus: A Study of the Relatives of 1241 Diabetic Propositi, Ann. Eugenics **15**: 95-119 (March) 1950.

1. Symons, N. S.: Read before the National Noise Abatement Symposium, Oct. 5, 1951.

2. Fox, M. S.: Industrial Noise: Its Medical, Economic, and Social Aspects, Am. J. M. Sc. **223**: 447 (April) 1952.

THE PRESIDENT'S PAGE

A MONTHLY MESSAGE

I have previously commented on the fact that too many members of the American Medical Association know too little about their organization or its activities. Recently, additional evidence for such a comment stemmed from rumors circulated by nonmedical persons. These rumors should never have arisen, but, when they did, they should have been squelched immediately, as there were no sound reasons for their origin. For example, I have recently heard a rumor that the American Medical Association had made a large contribution to the campaign of a political candidate. The rumor is, of course, ridiculous. The American Medical Association neither ethically nor legally could make such a contribution. It never has done so, and I am sure it never will.

The Association is made up of physicians from all regions of the country and of various political faiths. Its members as individuals are free to support any party or any candidate, but as an organization they cannot and should not. It is just as absurd to think that the Association would or could contribute to a political organization as to think it would contribute to any one religious group. Members of the Association ought to know this and be prepared to answer immediately any absurd charges to the contrary. But, if they do not know the facts concerning any situation, they should ask for them from the headquarters of the American Medical Association. Then they can answer with authority as well as conviction.

Recently a statement that the Association had brought to a close its National Educational Campaign because it had accomplished its purpose resulted in many letters and telephone calls being received by the Association's headquarters and its officers belaboring them because they had ceased their opposition to compulsory health insurance. Such cessation of opposition was never said nor implied, as a careful reading of the statement would reveal (see THE JOURNAL, Oct. 4, pages 494-495). In fact, physicians could have helped, individually, to counteract the effects of such rumors. The Association has not, and in my opinion never will cease its opposition to compulsory health insurance.

Nearly five years ago the Association embarked on a campaign to enlighten the public on the dangers of compulsory health insurance. Congress gave us support, and about 11,000 organizations, local, state and national, endorsed our stand. As a result the immediate danger has passed. We have won a breathing space, and that particular type of campaign seemed no longer necessary; hence, it was brought to a close. The long-range danger still exists, and we must remedy any weaknesses in our medical care system during this breathing space. We are bending every effort to do so.

One of the newer threats we face is the convention adopted by the recent International Labor Conference. This is an outright threat to personal freedom for everyone, a fact that must be appreciated by all people and especially by the medical profession (see THE JOURNAL, Aug. 23, pages 1572 and 1574). Perhaps then a new campaign may be essential, but we must remember that any war consists of various campaigns and often of numerous battles. We have won a battle and possibly a campaign, but we have not won the war, which for physicians, especially, concerns health matters.

Knowing the militant attitude of the American Medical Association toward the protection of freedom in medicine, it is difficult for me to understand how anyone could think that the Association had quit fighting for the principles in which it believes. Again, were there doubt in anyone's mind, a telephone call or letter asking for information would have relieved all fears.

Still another rumor which is absolutely incredible has been circulated. This is to the effect that the American Medical Association intends to employ a lawyer to defend those physicians who entered into an arrangement with pharmacists from which they profited financially at the expense of the public and who were so widely publicized recently in the New York press. How anyone could start such a rumor or give credence to it is inconceivable to me. The American Medical Association has always stood four-square against fee-splitting, "kick-backs," exorbitant fees, and any other form of unethical conduct.

Any physician who would write a code prescription to be filled by a druggist for which the patient would pay an increased fee, with the physician then receiving a kick-back as a result of this increased fee, is a disgrace to the medical profession. He is not worthy of the name "doctor." While it is possible that some physicians have been unjustly accused and should, therefore, be cleared of the charge, nevertheless they should be able to produce incontrovertible evidence that they are not guilty. Any physician who is guilty should pay an extreme penalty, and the members of his profession should have no sympathy for him.

There are honorable traditions in the medical profession, and these traditions must be upheld. We have asked the support of the public in our fight against infringement on medical practice. We cannot expect the public to support us unless we are true to our heritage. Our profession is one of service, not selfish gain. It is one that considers the interests of the patient first, last, and always, and not the fullness of the physician's pocketbook. Therefore, may I urge that, whenever one hears a rumor to this or that effect, that it not be spread further, but that the true facts be ascertained from the local, state, or national association, and then if there is no basis for the rumor that he do his part in stopping its further progress. Such absurd rumors as I have cited do much harm to the Association and the cause of medicine.

Further, we must inculcate the newly trained physician in the ethics and traditions of the medical profession. I suggest that each county medical society, before admitting anyone as a member, be satisfied that the applicant is thoroughly familiar with these matters. Copies of the Principles of Medical Ethics can always be obtained from the office of the Secretary of the American Medical Association in Chicago. I also suggest that the new member be given instruction in how medicine is organized and works. Too many physicians, and not only recent graduates, do not have a working knowledge of the functioning of local, state, and national associations. How can they hope to work harmoniously, participate in local medical activities, or claim the right to criticize those working in behalf of their interests and those of their association is difficult to understand. We have no more important task in the immediate future than that of making sure that medicine remains true to its high ideals and traditions.

There is an old Roman tradition that the height of idealism was to be "as pure as Caesar's wife." The great bulk of our profession meets that standard in matters of medical ethics and public relations. Unfortunately, that great mass of physicians is having their integrity besmirched by a small group lacking in morals, ethics, or anything approaching integrity. There is only one group that can get rid of these malefactors who bring discredit on our profession and that is the profession itself. These malefactors deserve and should receive neither sympathy nor consideration.

I have written frankly in this message because I believe frankness is indicated when it is necessary to dispel confusion. I have not intended, however, to cause offense. Judgment of any person's actions must rest with that person and his colleagues. I firmly believe that only a small percentage of our profession is guilty of thoughtless action, and I believe equally firmly that this problem is one for the profession to recognize and solve. It should not, however, be a subject for presentation in such a way that more publicity than action stems from the presentation. There is no reason for the profession to hide that it is trying to police its own ranks, but it is not wise for its own members to issue publicly statements that may be misunderstood and reported erroneously to the public. We do not have to decry publicly our problems to cope with them. Such discussions should be between physicians and before medical societies where they will result in proper action, which when indicated should be disciplinary.

LOUIS H. BAUER, M.D., Hempstead, N. Y.

MEDICAL NEWS

CALIFORNIA

San Francisco and Antioch Begin Fluoridation.—California's third and fourth cities to fluoridate their public water supplies recently began operation. Initially, about one third of San Francisco's area, practically all of which is residential district, will receive the fluoridated water. This is about 70% of the total population.

Outbreak of Malaria.—According to Dr. Wilton L. Halverson, State Director of Public Health, California's first outbreak of locally acquired malaria since 1945 has resulted in at least 10 cases of the disease among campfire girls who attended summer camp in a remote area of Nevada County. All cases were of the Plasmodium vivax type. Source of the original infection apparently was a Korean veteran who had a malaria relapse while camping near the area where the other cases subsequently occurred.

Morris H. Nathanson Memorial Lectures.—The Nathanson lectureship in cardiovascular and renal physiology and pharmacology has been established at the University of Southern California in memory of the late Dr. Morris H. Nathanson, who for more than 15 years served as associate clinical professor of medicine in the School of Medicine. While more than $5,000 has already been collected, it is anticipated that $25,000 will be needed. Contributions payable to the University of Southern California should bear on the face of the check the following notation: "To apply on the Morris H. Nathanson Lectureship Fund in Physiology and Pharmacology," and should be sent to Paul R. Saunders, Ph.D., Department of Pharmacology, University of Southern California School of Medicine, Los Angeles.

COLORADO

Lecture by Dr. Churchill.—The annual Harvard lecture will be delivered at the University of Colorado Medical Center, Denver, Nov. 7 at 5 p. m. by Dr. Edward D. Churchill, John Homans professor of surgery at the Harvard Medical School, Boston. An alumni dinner will be given in Dr. Churchill's honor at the University Club following his lecture. On Saturday Dr. Churchill will conduct a clinic at 8 a. m. in the surgical amphitheater of the Denver General Hospital.

Faculty Promotions.—The University of Colorado School of Medicine, Denver, announces the following promotions of full-time faculty members: Dr. Edith Boyd to professor of physical growth; Dr. James Flett Jr. to associate professor of medicine; Dr. Jerome W. Gersten to associate professor of physical medicine and rehabilitation; Dr. John H. Githens to assistant professor of pediatrics; Dr. Seymour Levine to assistant professor of biophysics; Dr. Robert W. McCammon to assistant professor of pediatrics; and Dr. George C. Twombly Jr. to assistant professor of physical medicine and rehabilitation. Volunteer faculty promotions include: Dr. Spencer Bayles to assistant clinical professor of psychiatry; Dr. C. Delmar Bonham to senior clinical instructor in obstetrics and gynecology; Dr. John S. Bouslog to clinical professor of radiology; Dr. Harold G. Burden to clinical instructor in obstetrics and gynecology; Dr. Vincent G. Cedarblade to assistant clinical professor of surgery; Dr. Raymond C. Chatfield to assistant clinical professor of obstetrics and gynecology; Dr. Gerard W. Del Junco to assistant clinical professor of obstetrics and gynecology; Dr. Elmer M. Franz to clinical instructor in orthopedic surgery; Dr. John E. Gardell to clinical instructor in orthopedic surgery; Dr. Murray E. Gibbens to clinical instructor in orthopedic surgery; Dr. Morris R. Gottesfeld to senior clinical instructor in obstetrics and gynecology; Dr. John B. Gramlich to assistant professor of anatomy (part time); Dr. John G. Griffin to assistant clinical professor of neurosurgery; Dr. Lewis L. Hall to assistant clinical professor of obstetrics and gynecology; Dr. Frederick R. Harper to clinical professor of thoracic surgery and head of the division of thoracic surgery; Dr. Dean W. Hodges to senior clinical instructor in obstetrics and gynecology; Dr. James C. Lombardi to clinical instructor in obstetrics and gynecology; Dr. Herbert R. Markheim to clinical instructor in orthopedic surgery; Dr. William Nelson to clinical instructor in orthopedic surgery; Dr. Paul M. Rice to assistant clinical professor of obstetrics and gynecology; Dr. Thaddeus P. Sears to associate clinical professor of medicine; Dr. Myron C. Waddell to senior clinical instructor in obstetrics and gynecology; and Dr. Ben C. Williams to assistant clinical professor in obstetrics and gynecology. Dr. Atha Thomas, an associate clinical professor in orthopedics, has been named head of the department of orthopedic surgery.

CONNECTICUT

State Medical Election.—At the annual meeting of the Connecticut State Medical Society in Hartford, Dr. Edward J. Whalen, Hartford, was chosen president; Dr. George H. Gildersleeve, Norwich, president-elect; Dr. Thacher W. Worthen, Hartford, first vice-president; Dr. Carl C. Harvey, Middletown, second vice-president; Dr. Frank H. Couch, Cromwell, treasurer; Dr. Creighton Barker, New Haven, executive secretary; and Dr. Stanley B. Weld, Hartford, editor of the journal.

Lectures on Cardiovascular Disease.—The Stamford Heart Association is presenting a monthly series of lectures on cardiovascular disease for physicians in Fairfield County. There is no fee for this series, which is accredited and endorsed by the Stamford Academy of General Practice and Stamford Medical Society. The association has also initiated monthly cardiac clinic conferences at Stamford Hospital with Dr. Ruth Whittemore, associate clinical professor in pediatrics, and Dr. Harold M. Marvin, associate clinical professor of medicine, Yale University School of Medicine, New Haven, Conn., acting as consultants on alternate months. Physicians in the Stamford area are invited to attend. Information may be obtained from Mrs. Shirley K. Sarkin, Executive Secretary, Stamford Heart Association, Stamford Hospital.

DISTRICT OF COLUMBIA

Society News.—The Washington Medical and Surgical Society has elected Dr. George W. Reeves, president; Dr. John M. Orem, vice-president; and Dr. Emil J. C. Hildenbrand, secretary. Dr. Frank E. Gibson Sr., Bethesda, Md., is permanent treasurer.

Georgetown University Awards.—At its annual awards luncheon, held at the National Press Club, the Georgetown University Alumni Club presented certificates to Drs. Thomas F. Keliher, professor of internal medicine, Georgetown University School of Medicine, Washington, D. C., and Leo I. Donovan, Bethesda, Md., the most immediate past president of the alumni club. Dr. Donovan was an instructor at the Georgetown University School of Medicine before entering general practice. These alumni achievement awards are given because of "distinguished services rendered by the sons of Georgetown to our country, our city, and our Alma Mater."

FLORIDA

Cancer Grant.—The Dade County Cancer Institute was recently the recipient of a grant of $10,854 from the National Cancer Institute for cytochemical investigations of exfoliated cells. The proposed project, "The Study of Cytochemical Techniques Utilizing the Surface Cell-Biopsy Cytological Method in Carcinoma in Situ, in Neuro-Carcinoma (Anaplastic Precancer Cell State), and in Clinical Carcinoma of the Cervix," will be conducted under the direction of Drs. B. C. Hopman and J. Ernest Ayre, Miami.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education and public health. Programs should be received at least three weeks before the date of meeting.

Medical District Meetings.—Four medical districts will hold scientific assemblies at 2:30 p. m. as follows: Oct. 27, Panama City (A), St. Andrews Bay Yacht Club, "A Phase of Postpartum Bleeding with Case Reports" and "Thoracic Problems of Interest to the General Practitioner"; Oct. 29, St. Petersburg (C), Detroit Hotel, "Management of Thoracic Problems in General Practice" and "The Female Urethra in the Diagnosis of Abdominal and Pelvic Pain"; Oct. 30, Fort Pierce (D), Flamingo Restaurant, "Diabetic Neuropathy" and "Early Diagnosis and Management of the Common Neoplasms"; Oct. 31, Daytona Beach (B), Daytona Beach Gun Club, "Problems in Sterility" and "Management of the Ambulatory Cardiac."

GEORGIA

Joint Meeting in Columbus.—The Georgia Urological Association and the Georgia Chapter of the American College of Surgeons will meet at the Ralston Hotel in Columbus, Oct. 28, and on Oct. 29 the Georgia State Obstetrical and Gynecological Society will meet in the same place. Guest speakers include Drs. Harold L. Foss, Danville, Pa., Edward D. Churchill, Boston, Grant E. Ward, Baltimore, Parke G. Smith, Cincinnati, and Lester A. Wilson, Charleston, S. C. Tuesday at 6 p. m. there will be a subscription dinner for all groups with the Muscogee County Medical Society at the country club.

ILLINOIS

Meeting of Anesthesiologists.—The Illinois Society of Anesthesiologists and the Chicago Society of Anesthesiologists will hold a joint meeting Oct. 31 at the Congress Hotel in Chicago. Ivan W. Magill, England, will be the guest speaker. Dinner at 6 p. m. will be followed by the meeting at 8 o'clock.

Chicago

Dr. Sanford Succeeds Dr. Poncher.—Dr. Heyworth N. Sanford, a member of the faculty of the University of Illinois College of Medicine since 1941, has been appointed acting head of the department of pediatrics to succeed Dr. Henry G. Poncher, who resigned Aug. 31 (*J. A. M. A.* **148:**1040 [March 22] 1952). Dr. Sanford was affiliated with Rush Medical College from 1928 until it was merged with the University of Illinois in 1941 and has served as chairman of the department of pediatrics at Presbyterian Hospital since 1946 and as president of the medical staff at Presbyterian since 1947. During the past four years he has been head of the department of children's hematology at Cook County Hospital, to which he came in 1930. Dr. Sanford was a member of the Department of the Interior's Commission to Puerto Rico, the Virgin Islands, and the Dominican Republic in 1948, and in 1950 he served as a member of the American Medical Association's Committee to England to study the National Health Act. He is a past president of the Chicago Pediatric Society. He served as medical director of the Infant Welfare Society of Chicago from 1928 to 1948.

Personals.—Dr. Harry A. Waisman, assistant professor of pediatrics, University of Illinois College of Medicine, has been appointed associate professor of pediatrics at the University of Wisconsin Medical School, Madison.——Dr. Richard A. Perritt lectured on "A Technique of Corneal Resection for the Restoration of Vision Employing the Binocular Dissecting Microscope" before the meeting of the International College of Surgeons held in Madrid and Barcelona, Spain.——Dr. Josiah J. Moore has been appointed a member of the Chicago Board of Health. ——Dr. Irving F. Stein was recently elected president of the American Society for the Study of Sterility.——Dr. Aldo A. Luisada, associate professor, department of medicine of the Chicago Medical School, delivered two lectures at the Academy of Medicine in Turin, Italy, on heart surgery.——Dr. Piero P. Foa, professor of physiology and pharmacology, Chicago Medical School, attended the Second International Congress of Biological Chemists at the Sorbonne in Paris recently, where he read two papers describing work that he and his associates have done with pancreatic extracts in experimental diabetes. In Milan, Italy, he lectured on endocrinology of the pancreas at the University of Milan Medical School and at the Lombardy Academy of Medical and Biological Science.——Dr. J. P. Greenhill was recently the guest of the Scandinavian Obstetrical and Gynecological Society in Copenhagen. He addressed medical groups in Stockholm on "Use of Androgens in Gynecology."——Dr. J. Garrott Allen, professor of surgery, University of Chicago, addressed the San Francisco Medical Society Oct. 14 on "Ulcerative Colitis—A Medical and Surgical Problem."

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INDIANA

State Medical Meeting in Indianapolis.—The Indiana State Medical Association will hold its annual session in Murat Temple, Indianapolis, Oct. 28-30, under the presidency of Dr. J. William Wright, Indianapolis. The annual golf tournament will start at 10 a. m. Tuesday at the Meridian Hills Country Club and the annual trap shoot at the same time at the Indiana Gun Club. Dr. John Rock, Boston, will talk at 10: 45 a. m. Wednesday on "Human Infertility," and at 11:15 a. m. Dr. William B. Tucker, Minneapolis, will speak on "Chemotherapy in Tuberculosis." At 2 p. m. the section on surgery will conduct a panel discussion on "Acute Abdominal Emergencies" (Murat candidates room), and the section on general practice will have a panel discussion on "Health Insurance as It Relates to the General Practitioner" (Egyptian room). "Obstetric Hemorrhage" will be the subject of a panel discussion held at the same time by the section on obstetrics and gynecology (East room, Athenaeum), which will offer a panel discussion on "Gynecologic Hemorrhage" at 3 p. m. At 2:30 p. m. in the Little auditorium of the Athenaeum, the section on preventive medicine and public health will hold a panel discussion on "Purposes and Organization of the Section on Preventive Medicine and Public Health." Guest speakers during the afternoon session will include Dr. George J. Thomas, Pittsburgh, who will discuss "Fire and Explosion Hazards in Hospitals, and Their Controls"; Dr. Haven Emerson, New York, who will speak on "Roles of the Family Physician and the Local Health Officer in the Public Health Program"; and Dr. Thomas Francis Jr., Ann Arbor, Mich., who will present "New Developments in Virus Diseases." On Thursday at 11 a. m. Dr. Paul W. Schafer, Kansas City, Kan., will address the general meeting on "Treatment of Shock in Major Disaster Without Blood or Plasma," and at 11:30 a. m. Dr. Bruce K. Wiseman, Columbus, Ohio, will discuss "Problems and Dangers of Transfusion." The program for Thursday evening includes addresses by Drs. Victor M. Sborov, Washington, D. C., "Infectious Hepatitis"; Arthur J. Patek Jr., New York, "Cirrhosis of the Liver"; and Robert M. Zollinger, Columbus, Ohio, "Indications for Surgery in Jaundiced Patients." The annual dinner and dance will be given at 6:30 p. m. in the Indiana ballroom. The program includes recognition of 50-Year Club members, an award to the general practitioner of the year, an address by Dr. Edward J. McCormick, Toledo, Ohio, President-Elect of the American Medical Association, and presentation of a certificate of merit and plaque to Dr. Wright. The Woman's Auxiliary to the Indiana State Medical Association will hold its meeting simultaneously with that of the parent organization.

MAINE

State Society's Clinical Session.—The Fall Clinical Session of the Maine Medical Association will be held in Waterville Oct. 26-27 at the Elmwood Hotel under the presidency of Dr. Eugene H. Drake, Portland. On Sunday, dinner at 6 p. m. will precede a panel on poliomyelitis, presented through the courtesy of the Maine Department of Health and Welfare. "Implications of Current Research on Poliomyelitis" will be discussed by Joseph L. Melnick, Ph.D., associate professor of microbiology, Yale University School of Medicine, New Haven, Conn., and "Clinical Aspects of Current Research on Poliomyelitis" by Dr. Robert Ward, professor of pediatrics, New York University College of Medicine. On Monday clinics will be held in the Central Maine Sanatorium in Fairfield, Sisters' Hospital, and Thayer Hospital, Waterville. At Thayer Hospital there will be a round-table discussion on diagnosis of cardiac disease at 11 a. m. Medical motion picture films will be shown throughout the day at Sisters' and Thayer hospitals. At 7 p. m. Dr. Ernest E. Huber, Natick, Mass., U. S. Public Health Service, will address the dinner meeting on "What Is Expected of Our Profession Today in the Light of National Events." The Woman's Auxiliary to the Maine Medical Association will hold its meeting at the same time.

weeks before the date of meeting.

Ayre, Miami.

MASSACHUSETTS

Commemorative Stamp Series.—A stamp honoring Louis Pasteur has been issued by the Worcester Foundation for Experimental Biology, Shrewsbury, as the first of an annual series commemorating "Heroes of Science." These stamps are for decorative and collection use only. Proceeds will be used to further research projects at the foundation in cancer, schizophrenia, arthritis, arteriosclerosis, hypertension, and many other fields. Contributions for the stamps are entirely voluntary.

New England Center Lectures.—The House Officers' Association of New England Center Hospital announces the following programs in its evening lecture series:

Oct. 29, Cause of Delay in Coagulation of Blood in Hemophilia, Leandro M. Tocantins, professor of clinical and experimental medicine, Jefferson Medical College of Philadelphia.
Nov. 19, Dyspnea, Eugene A. Stead Jr., professor of medicine, Duke University School of Medicine, Durham, N. C.

These programs will be held at 7 p. m. in the Stearns auditorium of New England Center Hospital. All interested persons are invited to attend.

Personals.—Dr. Anthony V. Pisciotta, Boston, has assumed his duties as head of the hematology service at the Milwaukee County General Hospital and as instructor in medicine at Marquette University School of Medicine, Milwaukee. He also will conduct a research program in leukemia under a grant by the Milwaukee division of the American Cancer Society.——Dr. Merrill Moore, Boston, recently gave a lecture on "The Development of the Sonnet Form" at the Harvard Club of Boston and read selections from his three recent books, "Clinical Sonnets," "Illegitimate Sonnets," and "Case Record from a Sonnetorium," as well as from his newest book, "More Clinical Sonnets," which will soon be published.

MINNESOTA

Tuberculosis Course for Laymen.—The University of Minnesota in conjunction with the Minnesota Public Health Association will present a continuation course in tuberculosis for lay persons at the Center for Continuation Study on the University of Minnesota campus, Minneapolis, Oct. 27-29. Emphasis will be placed on the public health aspect of tuberculosis.

Fall Refresher Course.—The Minnesota Academy of General Practice will hold its annual fall refresher at the Hotel Radisson in Minneapolis, Oct. 29, beginning at 8:20 a. m. Speakers will include Drs. Philip Thorek and Philip Lewin, Chicago, Dr. Arthur C. Corcoran, Cleveland, Dr. John E. Estes, Rochester, Minn., and Drs. Elexious T. Bell and Cecil J. Watson, Minneapolis.

Course in Medical Economics.—A continuation course in "Medical Economics for Physicians" will be presented by the University of Minnesota Oct. 30 and 31 in the auditorium of the Museum of Natural History, which is adjacent to the Center for Continuation Study. A partial list of subjects to be presented includes the business aspects of medical practice, the physician and the law, investments, and office planning. At noon on Friday, after the conclusion of the course, a homecoming program for physicians, presented at the staff meeting of the university hospitals, will feature the role of the medical school in relation to medical practice in the state. On Friday afternoon and Saturday morning, homecoming clinics will be held at the university hospitals and will include the presentation of surgical, medical, pediatric, dermatological, and gynecologic cases. All physicians are invited to attend this homecoming program.

NEW JERSEY

George T. Pack Lectureship Established.—The Medical Board of the Paterson General Hospital announces that it will sponsor an annual lecture on neoplastic diseases in honor of Dr. George T. Pack of the hospital staff. This lecture, which is to be given by Dr. Pack or some other authority on neoplastic diseases, is to be known as "The George T. Pack Annual Lecture on Neoplastic Diseases of the Paterson General Hospital."

NEW YORK

Nassau Physicians Form Academy.—The Nassau County Medical Society recently announced plans for the establishment of a Nassau County Academy of Medicine and the construction of an academy building. The preliminary plans call for a one story structure with office space, lobby, library, board room, and two secondary conference rooms and allow for expansion of the building when needed.

Personals.—Dr. Robert Collier Page received a gold medal from the Argentine Medical Association during his recent tour of South America. The award was a tribute to him "as a medical man, scientist, organizer, and writer for his work towards a better understanding regarding modern medicine between the nations of the Western Hemisphere."——Dr. Lewis K. Dahl, formerly assistant physician to the Hospital of the Rockefeller Institute for Medical Research in New York, has joined Brookhaven National Laboratory, Upton, L. I., as chief of the medical research division in the hospital.——Dr. Robert E. Plunkett, director, Division of Tuberculosis Control, State Department of Health, has been reappointed to the Committee on Tuberculosis of the Division of Medical Sciences, National Research Council, Washington, D. C., for the seventh year.——Dr. Curtis J. Lund, for the past five years a member of the faculty of the Louisiana State University School of Medicine, New Orleans, has been appointed professor of obstetrics and gynecology at the University of Rochester School of Medicine and Dentistry to succeed Dr. Karl M. Wilson, who retired in June after serving on the Rochester medical faculty for 27 years.——Benjamin M. Duggar, Ph.D., Pearl River, discoverer of aureomycin, celebrated his 80th birthday Sept. 1. Dr. Duggar, who is emeritus professor of the University of Wisconsin, Madison, has taught also at Radcliffe College, Harvard, Cornell, University of Missouri, and Washington University in St. Louis. In 1944 he was awarded the honorary degree of doctor of laws by the University of Missouri at Columbia. He is still actively engaged in research and laboratory work.——Dr. Robert H. Broad, Binghamton, former president of the New York State Health Officers Association, has been appointed Tompkins County health commissioner.

New York City

Herman L. Reiss Memorial Lecture.—The New York Institute of Clinical Oral Pathology announces the first Herman L. Reiss memorial lecture, to be held at the New York Academy of Medicine Oct. 27 at 8:30 p. m. The essayist will be Prof. Robert V. Bradlaw, F.R.C.S., England, University of Durham, Newcastle-upon-Tyne, England, who will lecture on "Oral Syphilis."

Tuberculosis Conference.—The Tuberculosis Sanatorium Conference of Metropolitan New York will hold a clinical session on "Pulmonary Calcifications" Oct. 29, 8:15 p. m., in the Cornell University Medical College Amphitheatre, 1300 York Ave. (at 69th St.). Presentations on "Tuberculous Calcification" by Dr. Robert G. Bloch, Montefiore Hospital for Chronic Diseases, and on "Nontuberculous Calcification" by Dr. Coleman B. Rabin, Columbia University, will be discussed by Drs. G. Arnold Cronk, Syracuse University, Leon Sokoloff, New York University College of Medicine, and Henry K. Taylor, New York University Post-Graduate Medical School.

Alumni Conference of Hospital for Joint Diseases.—The alumni of the Hospital for Joint Diseases will hold their annual conference at the hospital, Oct. 30 to Nov. 1. Thursday will be given over entirely to Dr. Joseph Trueta, Nuffield professor of orthopedic surgery of the University of Oxford, England. He will devote one session to a follow-up clinic and panel discussion on acute and chronic pyogenic osteomyelitis, another to a talk on "Acute Hematogenous Osteomyelitis, Its Pathology and Treatment," and the evening session to the annual Walter M. Brickner lecture on "The Influence of the Blood Supply in Controlling Bone Growth." Friday morning Dr. Anthony F. DePalma, professor, department of orthopedic surgery, Jefferson Medical College of Philadelphia, will conduct a panel discussion on the shoulder-neck pain syndrome. There will also be panel discussions on the present day status of work on the autonomic nervous system and on myelography.

OHIO

Sixth District Postgraduate Day.—The Sixth Councilor District Postgraduate Day will be held Oct. 29 at the Hotel Pick-Ohio, Youngstown. Physicians from the Mayo Clinic will make the following presentations:

Oliver H. Beahrs, (1) Surgical Conditions of the Female Pelvis and (2) Diagnosis of the Acute Surgical Abdomen.
Lloyd E. Harris, Abnormalities in the Newborn Period
Arthur M. Olsen, Common Pulmonary Diseases.
Howard F. Polley, ACTH and Cortisone in Arthritis.
Charles H. Scheifley, (1) ACTH and Cortisone in Rheumatic Fever and (2) Treatment of Chronic Congestive Heart Failure.

At dinner (6:30 p. m.) Tennyson Guyer, Ph.D., LL.D., Findlay, will have as his subject "That's the Spirit."

OKLAHOMA

Clinical Conference.—The Oklahoma City Clinical Society will hold its annual fall clinical conference at the Oklahoma Biltmore Hotel, Oklahoma City, Oct. 27-30. Dr. George F. Lull, Secretary and General Manager of the American Medical Association, Chicago, will be guest of honor at a dinner given by the Oklahoma County Medical Society at 7 p. m. Monday in the Civic Room of the Biltmore Hotel. He will speak on "What Happens to Your American Medical Association Dues." Guest lecturers will serve as moderators for panel discussions as follows:

Oct. 27, 2:45 p.m., Rubin H. Flocks, Iowa City, Carcinoma of the Prostate.
John B. Bartram, Philadelphia, and William L. Riker, Chicago, Congenital Lesions of the Gastrointestinal Tract.
Oct. 28, 9:45 a.m., Rolland J. Whitacre, Cleveland, Use and Abuse of Pentothal and Curare.
James A. Dickson, Cleveland, Delayed and Early Nonunion, Fractures of the Neck of the Femur (Treatment and End Results That Can Be Expected).
2:45 p.m., Roscoe L. Pullen, Houston, and Joseph B. Vander Veer, Philadelphia, Pulmonary Embolism, Treatment and End Result.
John H. Randall, Iowa City, and Lewis C. Scheffey, Philadelphia, Vaginal Discharge and Its Treatment.
Oct. 29, 9:45 a. m., Howard K. Gray, Rochester, Minn., Management of Ulcerating Lesions of the Stomach.
Clarence S. Livingood, Galveston, Texas, Management of Pruritis.
2:45 p.m., Francis L. Lederer, Chicago, Current Status and Management of Malignancies About the Head and Neck.
Edwin L. Rippy, Dallas, Management of Complications in the Diabetic Patient.
Oct. 30, 9:45 a.m., Newton D. Smith, Rochester, Minn., Tumors and Cysts in the Peri-Anal, Anal, and Rectal Regions.
John R. Schenken, Omaha, and Harvey White, Chicago, Differential Diagnosis and Pathology of Abdominal Tumors in Children.

The annual clinic dinner dance given by the Oklahoma City Chamber of Commerce will be held on Tuesday at 7:30 p. m. in the Persian Room of the Skirvin Tower Hotel. Wednesday at 7:30 p. m. the women physicians' annual dinner will be held in the President's Room of the Oklahoma Club, while the clinic smoker will start at 8 p. m. in the Civic Room of the Biltmore Hotel. On Thursday (12:15 to 1:40 p. m.) the medical and surgical groups will have a combined round-table luncheon on the seventh floor of the Oklahoma Club. On the other days of the session these groups will hold separate round-table luncheons, 12:15 to 1:40 p. m., the medical group meeting in the Oklahoma Club and the surgical group in the Mirror Room of the Biltmore Hotel.

The clinical conference is classified as a formal study course by the American Academy of General Practice. Academy members will receive credit for the actual hours of attendance toward the 50 hours of formal postgraduate study required every three years.

PENNSYLVANIA

Hospital Training Course.—The Medical Society of the State of Pennsylvania in cooperation with the county medical societies will conduct a rotating postgraduate hospital training course for general practitioners. Individualized instruction, limited to four students on each service, will be given one day a week (9:30 a. m. to 4:15 p. m.) for 20 weeks and will include participation in ward rounds, clinics, and staff conferences. The courses will be given on Wednesdays, beginning Nov. 5 at the Albert Einstein Medical Center, Northern Division, Philadelphia; St. Joseph's Hospital, Reading; and Robert Packer Hospital, Guthrie Clinic, Sayre. On Thursdays beginning Nov. 6 the course will be given at the Harrisburg Polyclinic Hospital. The maximum enrollment at each hospital is 16 physicians; registration fee, $35. Applications should be sent to the Commission on Graduate Education, 230 State St., Harrisburg. Checks should be made payable to the Medical Society of the State of Pennsylvania.

Philadelphia

Symposium on Pediatric Allergy.—This symposium will be presented by the Philadelphia Allergy Society, Oct. 29, 8:30 p. m., at the College of Physicians, 19 S. 22nd St. Dr. Jerome Glaser, Rochester, N. Y., guest speaker, will discuss "Strained Meats as a Protein Base in Milk Allergy of Early Infancy," Dr. Louis E. Silcox, "The Role of Bacteria in Respiratory Allergy in Children," and Dr. Harold I. Lecks, "The Frequency of Food Allergy in the Asthmatic Child." A panel discussion on "Asthma in Children" will have as participants Drs. Jerome Glaser (foods), Louis Tuft (inhalants), Jean Crump (infection), and Howard C. Leopold (pollens).

Personals.—Dr. Irving H. Leopold has been appointed an attending surgeon at the Wills Eye Hospital, succeeding the late Dr. Louis Lehrfeld, who died on Feb. 6.——Dr. James P. Dixon, health commissioner of Philadelphia, has been elected president of the Association of the Alumni of the Columbia University School of Public Health.—Dr. Hobart A. Reimann, professor of medicine, Jefferson Medical College of Philadelphia, was recently appointed visiting professor of medicine at the American University of Beirut, Lebanon.——Dr. Francis C. Dohan, assistant professor of clinical medicine, University of Pennsylvania since 1947, was recently appointed medical director of RCA Victor Division, Radio Corporation of America, Camden, N. J. He will continue his research and teaching activities and limited private practice.

TEXAS

Obstetric and Gynecology Conference.—The Dallas Southern Clinical Society with the cooperation of the Southwestern Medical School of the University of Texas, Dallas, will present a conference on obstetrics and gynecology, Nov. 3-5, at the Baylor University Hospital. Dr. Albert W. Diddle, Knoxville, Tenn., honor guest speaker, will discuss the following subjects: "Dystocia and Prolonged Labor," "Woman," "Vaginal Bleeding," and "Ovarian Tumors." There will be daily round-table luncheons at 12 noon, and on Wednesday at 5:30 p. m. cocktails and dinner with the Dallas-Fort Worth Obstetric and Gynecologic Society will be served in the Texas Room of the Baker Hotel.

WASHINGTON

Lecture on Constructive Pericarditis.—Dr. C. Sidney Burwell, research professor of clinical medicine, Harvard Medical School, Boston, will speak on "Constructive Pericarditis," Oct. 28, at 3:30 p. m. in the auditorium of the Madigan Army Hospital, Fort Lewis.

Annual Heart Symposium.—The Washington Heart Association will present its fourth annual symposium in cooperation with the Washington State Department of Health, Nov. 7-8, at the University of Washington Medical School Auditorium, Seattle. "Hypertension" and "The Arrhythmias" will be discussed by Drs. Robert W. Wilkins, Boston, Eugene B. Ferris, Cincinnati, Stanley E. Bradley, New York, and Myron Prinzmetal, Los Angeles. Topics to be considered include renal adrenal humoral factors; neurogenic psychogenic factors; kidney function tests and renal insufficiency; diets; and surgery and drugs. No registration fee.

WEST VIRGINIA

Heart Association Meeting.—After the annual luncheon of the directors of the West Virginia Heart Association at the Hotel Morgan in Morgantown, Oct. 31, the following program will be presented at 2 p. m.:

Harold Feil, Cleveland, Surgical Approach to Heart Disease.
Claude S. Beck, Cleveland, Operations on the Heart with Special Emphasis on the Coronary Problem.
Herman K. Hellerstein, Cleveland, Evaluation of the Fitness of the Person with Heart Disease.

WISCONSIN

Misericordia Hospital Dedicates New Wing.—Misericordia Hospital, Milwaukee, dedicated its new million dollar wing Sept. 7. The seven story brick and steel addition includes an administration department, operating rooms, x-ray rooms, laboratories, an outpatient department, cafeteria, and 75 patient rooms. The wing was built with private funds only. Physicians and citizens, who donated more than $110,000 to furnish the new addition, celebrated the dedication with a dinner at the Schroeder Hotel.

ALASKA

Dr. Carswell Returns.—After an absence of 12 years, Dr. John A. Carswell has returned to Alaska to become chief of the Medical Services Section, Alaska Department of Health. He will also serve as deputy commissioner of health. Dr. Carswell was formerly affiliated with the New York State Department of Health, the Division of Tuberculosis Control in Westchester County, and various tuberculosis sanatoriums. He served as health officer of Santa Barbara County in California and since 1946 has been chief of tuberculosis service at the Veterans Administration Hospital in Portland, Ore.

Medical Association News.—At its recent annual convention in Anchorage the Alaska Territorial Medical Association elected Dr. Philip H. Moore, Mount Edgecumbe, president; Dr. William M. Whitehead, Juneau, first vice-president; Dr. Asa L. Martin, Anchorage, second vice-president; and Dr. William P. Blanton, Juneau, secretary and treasurer. Dr. John W. Cline, San Francisco, Past President of the American Medical Association, who was the banquet speaker, also presented during the sessions papers on "Indications for Surgery in Gallbladder Disease" and "Treatment of Intra-Abdominal Injuries." Other speakers from outside Alaska included Dr. Harold C. Voris, Chicago, who presented a film on neurosurgery and a paper on "Management and Treatment of Head Injuries"; Dr. James T. Mason, Seattle, who discussed "Treatment of Injuries to Genitourinary Tract" and "Management of Urological Problems by General Practitioner"; Dr. Karl L. Schaupp, San Francisco, whose topics were "Hemorrhage in Pregnancy," "Hemorrhage During Labor and Postpartum Hemorrhage," and "Diagnosis and Management of Toxemias in Pregnancy"; and Dr. Elmer M. Rusten, Minneapolis, who spoke on "Recent Advances in the Treatment of Common Skin Disorders."

GENERAL

Allergists Invite Papers.—The American College of Allergists, which will hold its annual congress April 27-29, 1953, at the Conrad Hilton Hotel, Chicago, preceded by three days of an intensive graduate instructional course, announces that abstracts in duplicate of papers to be presented at this meeting should be sent to Dr. Giles A. Koelsche, Chairman, Program Committee, Mayo Clinic, Rochester, Minn., not later than Jan. 15, 1953. All papers must be submitted for publication in the *Annals of Allergy*.

Bone Registry Available.—Applications for the loan of its Registry of Bone Sarcoma are being accepted by the American College of Surgeons. Containing 2,400 cases, all with microscopic sections, the registry is being offered to a teaching institution where "its potential value and further development may be realized to a maximum degree." The registry, which is completely representative of neoplasia in bone, is indexed and cross filed. Requests for its loan should be made to Dr. Ian Macdonald, Chairman, Subcommittee on Registry of Bone Sarcoma, American College of Surgeons, 40 E. Erie St., Chicago 11.

Memorial Fund for Medical Research.—The Jane Coffin Childs Memorial Fund for Medical Research, with headquarters at 333 Cedar St., New Haven 11, Conn., has announced that $264,080 for support of cancer research projects and fellowships was appropriated between Nov. 19, 1951, and June 6, 1952. Fifteen awards were made, the largest ($123,500) going to Dr. Charles B. Huggins, director, Ben May Laboratory for Cancer Research, University of Chicago School of Medicine, for the five year period, Jan. 1, 1952, to Dec. 31, 1956, for investigation on hormonal control of human cancer.

Dogs for Research.—A recent survey by the National Society for Medical Research shows that the average cost of raising one dog for one year, or to the usual point of medical usefulness, is $125. In contrast to this figure, the cost for obtaining animals from the dog pound is under $10 per dog. These dogs would otherwise be destroyed by the pound. The University of Maryland estimated the cost of raising the dogs required by its medical school at $50,000 annually, but pays the local pound only $750 for the same number of animals. The University of Pittsburgh is the only school that raises its own animals for research use, having been forced to do so because pound dogs are not available.

Occupational Injuries.—In this year's edition of "Accident Facts" the National Safety Council reveals that occupational injuries in 1951 accounted for a loss of $2,650,000,000 and of 280,000,000 man-days of labor. Twenty-one pages of the 96 page book are devoted exclusively to occupational accidents, with discussion of the commonest sources of injury, part of the body most frequently injured, off-the-job problems, women in industry, and many other subjects. Detailed statistical information is provided also on accidents of all types: motor vehicle, transportation, home, farm, and school. Single copies of the book may be obtained from the National Safety Council, 425 N. Michigan Ave., Chicago 11, at 75 cents each. Prices are reduced for quantities.

Regional Meeting of Physicians.—A regional meeting of the American College of Physicians for Arizona and New Mexico will be held in Albuquerque, N. Mex., Oct. 29 in the auditorium of the United States Veterans Hospital. The following program will be presented during the afternoon:

Louis N. Katz, Chicago, Modern Electrocardiography.
Charley J. Smyth, Denver, ACTH and Cortisone in Rheumatoid Arthritis.
Gordon Meiklejohn, Denver, Antibiotic Therapy.
Erich P. Hausner, Santa Fe, N. Mex., Subacute Bacterial Endocarditis—Therapeutic Aspects.

At 6:30 p. m. there will be cocktails followed by dinner at the Albuquerque Country Club. Dr. Dwight L. Wilbur, San Francisco, will deliver the address.

Meeting of Obstetricians and Gynecologists in Boston.—The New England Obstetrical and Gynecological Society will hold its annual meeting Oct. 29 at the Hotel Somerset, Boston. From 8 to 10 a. m. operative clinics will be conducted at Boston Lying-in Hospital; Lahey Clinic, New England Baptist Hospital; and Massachusetts General Hospital, White Building 3-A. The morning session at the Hotel Somerset, which will begin at 10:30 a. m., will be devoted to panel discussions on "Gynecological Bleeding," with Dr. Roy J. Heffernan, Brookline, Mass., as chairman and Drs. George Van S. Smith, Brookline, Mass., and Michael J. Jordan, New York, as collaborators, and "Prenatal Care," with Dr. Alfred L. Potter, Providence, R. I., chairman, and Drs. Benjamin Tenney Jr., Boston, and Walter S. Jones, Providence, R. I., collaborators.

Communicable Disease in Canada.—The U. S. Public Health Service reports that bubonic plague, Rocky Mountain spotted fever, and tularemia have been discovered in 10 areas on the prairies of southern Alberta, Canada. Three collections from Lomond, Brooks, and Hanna this summer proved positive for bubonic plague. These are the first positive specimens since 1949. The infection was found in gophers and gopher fleas. The last human case of bubonic plague in Alberta occurred at Stanmore in 1937. Rocky Mountain spotted fever was found in Redcliff and in areas south of the city and west of Calgary. A total of four positive collections was the largest since 1944. There has been one suspected human case. Tularemia has been discovered in several areas southeast of Calgary. One human case, the first in that area in three years, was reported in Foremost.

Music Therapy.—The annual convention of the National Association for Music Therapy will be held at the Hotel Kansan, Topeka, Kan., Oct. 30 to Nov. 1 under the presidency of Mrs. Esther Goetz Gilliland of Chicago. On Thursday at 7:30 p. m. Dr. John M. Anderson, Topeka, will serve as moderator for a round-table discussion of "Psychiatric Concepts of Music

Therapy." Collaborators will be Dr. Louis S. Cholden, Dr. Joseph D. Noshpitz, Austin Des Lauriers, Ph.D., and Dr. Milton H. Miller of Topeka, and Dr. Ira M. Altshuler of Eloise, Mich. Others participating in the program include Drs. Ruth I. Barnard, Topeka, Lewis L. Robbins, Topeka, Thomas G. Lupo, Waco, Texas, Benjamin A. Cockrell, Memphis, Tenn., Rudolf Leiser, Eloise, Phineas S. Sparer, Memphis, Maxim Pollak, Memphis, Jules H. Masserman, Chicago, and Edward D. Greenwood, Topeka. Dr. Karl Menninger, Topeka, will be the speaker at the dinner, Friday, 6:30 p. m., in the Roof Garden.

Heart Association Awards.—The American Heart Association has approved 72 grants-in-aid totaling $361,522.50 for research into heart and blood vessel diseases being conducted at institutions in 20 states, the District of Columbia, Montreal, and Beirut, Lebanon. These awards raise to over 4 million dollars the combined totals spent by the association for cardiovascular research projects during the last four years. Included among the subjects receiving the attention of investigators are the further development and use of the mechanical heart-lung and the artificial kidney; the role of metabolism, the brain and nervous system, sex hormones, and other glandular factors in high blood pressure and hardening of the arteries; congestive heart failure and kidney disease; causes and treatment of rheumatic fever; the heart muscle and cardiovascular physiology; blood flow and the vessel walls; blood clotting; diet and drugs; cholesterol and other fatty substances associated with hardening of the arteries; correction of heart valve defects and other surgical problems; breathing difficulties; and heart sounds and rhythms.

Cancer Seminar.—The sixth annual meeting of the Southeastern States Cancer Seminar will be held at the Tampa Terrace Hotel, Tampa, Fla., Oct. 30 to Nov. 1. This seminar is sponsored by the Florida Cancer Council, which includes representatives of the state medical association; American Cancer Society, Florida division; American College of Surgeons; and the Florida State Board of Health. It is financed by the American Cancer Society, Florida division, and the Florida State Board of Health. Speakers and their subjects are as follows:

Chemotherapy, Cornelius P. Rhoads, New York.
Lip, Mouth, and Throat, John J. Conley, New York.
Skin, Joseph A. Elliott Jr., Charlotte, N. C.
Surgery, Clarence E. Gardner, Durham, N. C.
Pathology, Elson B. Helwig, Washington, D. C.
Gynecology, John L. McKelvey, Minneapolis.
Chemotherapy, Leon O. Jacobson, Chicago.
Radiology, Charles L. Martin, Dallas, Texas.
Radiology, W. Edward Chamberlain, Philadelphia.
Pathology, Hugh G. Grady, Washington, D. C.

Southwestern Medical Meeting.—The annual meeting of the Southwestern Medical Association will be held Oct. 30 to Nov. 1 at the Hilton Hotel in Albuquerque, N. Mex. Guest speakers and their first presentations will include:

Herbert W. Meyer, New York, Diseases of the Breast.
Edgar Burns, New Orleans, Minor Lesions of the Female Urethra and Bladder.
Louis H. Douglass, Baltimore, Post Partum Hemorrhage.
Louis N. Katz, Chicago, Modern Concepts—Etiology and Pathogenesis of Arteriosclerosis.
Alfred E. Maumenee, San Francisco, Problems in Ophthalmology that Should Be Recognized in General Practice.
Frederick D. Weidman, Philadelphia, Differential Diagnosis of the Specific Infectious Granulomas, with Special Reference to Fungus Granulomas.

Round-table luncheons will be held at 12:15 p. m. On Thursday at 7:30 p. m. there will be a smoker and buffet in the ballroom and on Friday at 8 p. m. a dinner dance at the Albuquerque Country Club. Saturday afternoon the University of New Mexico plays the University of Arizona (football) at 2 p. m. Golf and trap shooting have also been arranged for the same time.

Manuals for Multiple Sclerosis Patients.—The National Multiple Sclerosis Society has published four manuals for patients, written by Dr. Edward E. Gordon, medical director of the Institute for Crippled and Disabled. These manuals aim to promote a home program of rehabilitation, physical therapy, and recreation for patients under the supervision of the physician. Written in simple terms and amplified by illustrations, they describe exercises that can be performed in the home to strengthen muscles, improve coordination, and prevent atrophy from disuse. Although numerous exercises are described, Dr. Gordon recommends that the physicians should prescribe the type and duration of the exercises. A section of each manual is devoted to suggestions on efficient performance of functions essential to daily living. The patient manuals, which supplement the physician's manual on rehabilitation already distributed to 15,000 physicians by the society, will be sent without charge to multiple sclerosis patients at the request of physicians who specify the appropriate manual needed for the patient. Inquiries should be addressed to the National Multiple Sclerosis Society, 270 Park Ave., New York 17.

New England Postgraduate Assembly.—The annual session of the New England Postgraduate Assembly, which will be held at the Hotel Statler, Boston, Oct. 28-30, will feature daily luncheon panels at 12:15 p. m. in the Georgian room as follows:

Tuesday, "Medical Versus Surgical Treatment of Thyrotoxicosis" and "Indications for Caesarian Section."
Wednesday, "Treatment of Obesity" and "Back Pain."
Thursday, "Indications for Surgery of the Upper Gastrointestinal Tract" and "Management of Coronary Thrombosis."

On Wednesday at 8:15 a. m. there will be a breakfast meeting of the New Hampshire and Vermont Academies of General Practice. At 5:15 p. m. the New England Academy of General Practice will hold its annual meeting in Parlor B. There will be a continuation of the symposium on nutrition (2:15 to 5 p. m.), sponsored by the department of nutrition, Harvard School of Public Health, and at 7 p. m. the Harvard Club will hold a symposium dinner. The New England Obstetrical and Gynecological Society will meet at the Hotel Somerset on Wednesday and the New England Rheumatism Association, New England Diabetes Association, and the New England Pathological Society will hold evening meetings during the sessions of the assembly (time, place, speakers, and subjects to be announced).

Physicians Needed in Canal Zone.—The health bureau, Canal Zone, is urgently in need of physicians. Two specialists are needed in pediatrics, general surgery, obstetrics and gynecology, and eye, ear, nose, and throat treatment, and one specialist in urology, orthopedics, and radiology. There are also occasional vacancies for general practitioners in outpatient clinics.

Starting salaries range from $7,425 (Civil Service rating GS-11) to $10,450 (Civil Service rating GS-13), according to training, experience, and type of position. Free transportation to the Canal Zone is provided for the appointee, legal dependents, and household goods. Family housing is immediately available. There are good hospitals, schools, and churches under standard American living conditions. A two month vacation with pay (which includes time lost for illness) is allowed, and reduced rates are granted on Panama Line vessels between the Canal Zone and New York. Positions come under Civil Service. Applicants should write to Health Director, Balboa Heights, Canal Zone, or to Chief of Office, Panama Canal Company, Washington 25, D. C.

Postgraduate Course on Premature Infant.—The Louisiana State Department of Health and the Charity Hospital of Louisiana at New Orleans in cooperation with the Louisiana State University School of Medicine and Tulane University School of Medicine, New Orleans, announce a postgraduate course on the premature infant, to be held Nov. 5-19 at the Premature Infant Center, Charity Hospital of Louisiana, 1532 Tulane Ave., New Orleans 12. Consideration will be given to the problems involved in the care of prematures at delivery, in the nursery, and preparatory to discharge. The course will include lectures, nursery rounds, seminars, demonstrations, field trips, and clinical conferences on such problems as resuscitation, obstetrical management of premature labor, retrolental fibroplasia, erythroblastosis, infections, use of incubators, types and kinds of feeding, construction of premature nursery, transportation of prematures, and problems of parents. The course, though open to all physicians, is limited to 10. There are no tuition fees. Registrants will be assisted in arranging hotel or other accommodations, if desired. Applications and requests for information may be addressed to Dr. Elaine L. Allen, Premature Infant Center, Charity Hospital, New Orleans.

National Society for Crippled Children and Adults.—This organization will hold its annual convention at the Fairmont Hotel, San Francisco, Oct. 26-30 under the presidency of Mr. Davis E. Geiger, Ashland, Ky. There will be seminars on social and emotional adjustment, speech therapy, rehabilitation, special

education, sheltered workshop, and the buyers' clinic. Film theaters will be held in the Garden room Monday from 2 to 4 p. m., and Tuesday at 7:30 p. m. On Sunday at 12:30 p. m. there will be an Easter Seal luncheon and institute in the Nob Hill room. The annual meeting of the California Society of Crippled Children, Inc., will be held during the luncheon in the Venetian room Monday, 12:30 to 3:30 p. m., and the annual meeting of the board of trustees of the national society will be held in the Hunt room from 12:30 to 4 p. m. on Tuesday. On Wednesday, 12:15 to 2:15 p. m., there will be a parents' luncheon in the Venetian room. The president's dinner, Wednesday, 7:30 p. m., in the Gold ballroom, will be addressed by Robert G. Sproul, LL.D., president of the University of California, Berkeley. Among the physicians who will present papers during the sessions are Drs. Pauline G. Stitt, Oakland, Calif., William J. Wedell, San Francisco, Harry F. Dietrich, Los Angeles, and Meyer A. Perlstein, Chicago.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories, and possessions in the weeks ended as indicated:

Area	Oct. 4, 1952	Sept. 27, 1952	Oct. 6, 1951
New England States			
Maine	10	11	4
New Hampshire	2	..	1
Vermont	6	1	..
Massachusetts	25	32	14
Rhode Island	8	13	2
Connecticut	23	18	23
Middle Atlantic States			
New York	145	159	72
New Jersey	39	63	20
Pennsylvania	120	105	49
East North Central States			
Ohio	195	243	69
Indiana	108	110	17
Illinois	249	324	87
Michigan	252	256	68
Wisconsin	162	180	102
West North Central States			
Minnesota	321	370	34
Iowa	255	213	17
Missouri	81	114	51
North Dakota	20	37	6
South Dakota	49	57	8
Nebraska	115	117	21
Kansas	129	124	39
South Atlantic States			
Delaware	12	6	..
Maryland	26	12	5
District of Columbia	2	7	3
Virginia	35	35	13
West Virginia	42	26	16
North Carolina	15	25	11
South Carolina	13	30	3
Georgia	38	15	16
Florida	24	33	4
East South Central States			
Kentucky	71	102	17
Tennessee	36	38	31
Alabama	11	6	16
Mississippi	20	24	29
West South Central States			
Arkansas	16	26	9
Louisiana	26	17	27
Oklahoma	30	50	16
Texas	83	87	55
Mountain States			
Montana	13	15	7
Idaho	13	14	1
Wyoming	4	6	13
Colorado	49	46	44
New Mexico	22	21	5
Arizona	27	16	8
Utah	37	26	34
Nevada	6	6	2
Pacific States			
Washington	59	77	18
Oregon	30	29	20
California	153	197	145
Territories and Possessions			
Alaska	..	..	4
Hawaii	3	..	2
Puerto Rico	..	..	..
Total	3,230	3,539	1,272

MEETINGS

AMERICAN MEDICAL ASSOCIATION CLINICAL SESSION, Denver, Dec. 2-5. Dr. George F. Lull, 535 North Dearborn Street, Chicago 10, Secretary.

AMERICAN ACADEMY OF DERMATOLOGY AND SYPHILOLOGY, Palmer House, Chicago, Dec. 6-11. Dr. John E. Rauschkolb, P.O. Box 6565, Cleveland 1, Secretary.

AMERICAN ACADEMY OF OBSTETRICS AND GYNECOLOGY, Palmer House, Chicago, Dec. 15-17. Dr. Ralph A. Reis, 116 S. Michigan Blvd., Chicago 3, Secretary.

AMERICAN ACADEMY OF TROPICAL MEDICINE, Galveston, Texas, Nov. 13-15. Dr. Clay G. Huff, Navy Medical Research Institute, Bethesda 14, Md., Secretary.

AMERICAN ASSOCIATION OF MEDICAL CLINICS, Cosmopolitan Hotel, Denver, Nov. 30-Dec. 1. Dr. Edwin P. Jordan, Box 114, Charlottesville, Va., Executive Director.

AMERICAN PSYCHOANALYTIC ASSOCIATION, New Yorker Hotel, New York, Dec. 4-7. Dr. LeRoy M. A. Maeder, 1910 Rittenhouse Square, Philadelphia 3, Secretary.

AMERICAN SOCIETY OF ANESTHESIOLOGISTS, Philadelphia, Nov. 11-14. Dr. J. Earl Remlinger Jr., Suite 1101, 188 West Randolph Street, Chicago 1, Secretary.

AMERICAN SOCIETY FOR THE STUDY OF ARTERIOSCLEROSIS, Hotel Knickerbocker, Chicago, Nov. 9-10. Dr. O. J. Pollak, P. O. Box 228, Dover, Del., Secretary.

AMERICAN SOCIETY OF TROPICAL MEDICINE AND HYGIENE, Galvez Hotel, Galveston, Texas, Nov. 13-15. Dr. Quentin M. Geiman, 25 Shattuck St., Boston 15, Secretary.

ASSOCIATION OF AMERICAN MEDICAL COLLEGES, The Broadmoor, Colorado Springs, Colo., Nov. 10-12. Dr. Dean F. Smiley, 185 North Wabash Ave., Chicago 1, Secretary.

ASSOCIATION OF MILITARY SURGEONS OF THE UNITED STATES, Hotel Statler, Washington, D. C., Nov. 17-19. Dr. R. R. Sayers, Armed Forces Institute of Pathology, Washington 25, D. C., Secretary.

ASSOCIATION FOR RESEARCH IN NERVOUS AND MENTAL DISEASES, Hotel Roosevelt, New York, Dec. 12-13. Dr. Clarence C. Hare, 700 West 168th St., New York 32, Secretary.

ASSOCIATION OF STATE AND TERRITORIAL HEALTH OFFICERS, Washington, D. C., Dec. 8-11. Dr. John D. Porterfield, 306 Ohio Depts. Bldg., Columbus 15, Ohio, Secretary.

CONGRESS OF NEUROLOGICAL SURGEONS, Palmer House, Chicago, Nov. 6-7. Dr. Bland W. Cannon, 1092 Madison Ave., Memphis, Tenn., Secretary.

INDIANA STATE MEDICAL ASSOCIATION, Murat Temple, Indianapolis, Oct. 28-30. Mr. James A. Waggener, 23 E. Ohio St., Indianapolis 4, Executive Secretary.

INTERSTATE POST GRADUATE MEDICAL ASSOCIATION OF NORTH AMERICA, Public Auditorium, Cleveland, Nov. 10-13. Dr. Arthur G. Sullivan, 16 North Carroll St., Madison, Wis., Managing Director.

NASHVILLE MEDICAL ASSEMBLY, Iris Room, Hermitage Hotel, Nashville, Tenn., Oct. 29-31. Dr. W. G. Kennon Jr., 647 Doctors Bldg., Nashville 3, Tenn., Secretary.

NATIONAL ASSOCIATION FOR MENTAL HEALTH, Henry Hudson Hotel, New York, Nov. 17-19. Dr. George S. Stevenson, 1790 Broadway, New York, Medical Director.

NEW ENGLAND OBSTETRICAL AND GYNECOLOGICAL SOCIETY, Hotel Somerset, Boston, Oct. 29. Dr. Carmi R. Alden, 270 Commonwealth Ave., Boston 16, Secretary.

NEW ENGLAND POSTGRADUATE ASSEMBLY, Hotel Statler, Boston, Oct. 28-30. Dr. Laurence B. Ellis, 22 Fenway, Boston, Chairman.

NORTH PACIFIC SURGICAL ASSOCIATION, Spokane, Wash., Nov. 21-22. Dr. John A. Duncan, 509 Olive Way, Seattle, Secretary.

OKLAHOMA CITY CLINICAL SOCIETY, Biltmore Hotel, Oklahoma City, Oct. 27-30. Dr. N. L. Miller, 512 Medical Arts Bldg., Oklahoma City, Director of Clinics.

OMAHA MID-WEST CLINICAL SOCIETY, Hotel Paxton, Omaha, Oct. 27-31. Dr. Payson S. Adams, 1031 Medical Arts Bldg., Omaha 2, Director of Clinics.

POSTGRADUATE ASSEMBLY IN ENDOCRINOLOGY AND METABOLISM, Roney Plaza Hotel, Miami Beach, Fla., Nov. 3-8. Dr. Henry H. Turner, 1200 N. Walker Street, Oklahoma City 3, Okla., Secretary.

PUERTO RICO MEDICAL ASSOCIATION, Santurce, Dec. 10-14. Dr. Luis R. Guzman-Lopez, Box 9111, Santurce, Secretary.

RADIOLOGICAL SOCIETY OF NORTH AMERICA, Cincinnati, Dec. 7-12. Dr. Donald S. Childs, 713 East Genesee St., Syracuse 2, N. Y., Secretary.

SAN ANTONIO TUMOR SEMINAR, Annex 4, Brooke Army Hospital, San Antonio, Texas, Nov. 1. Dr. A. O. Severance, 205 Camden St., San Antonio 2, Texas, Secretary.

SOUTHERN ELECTROENCEPHALOGRAPHIC SOCIETY, Sorrento Hotel, Miami Beach, Fla., Nov. 10-11. Dr. Irving Pine, Columbus Receiving Hospital, Columbus, Ohio, Secretary.

SOUTHERN MEDICAL ASSOCIATION, Miami, Fla., Nov. 10-13. Mr. C. P. Loranz, 1020 Empire Bldg., Birmingham 3, Ala., Secretary.

SOUTHERN PSYCHIATRIC ASSOCIATION, White Sulphur Springs, W. Va., Nov. 2-5. Dr. N. M. Owensby, Medical Arts Bldg., Atlanta 3, Ga., Secretary.

SOUTHERN SURGICAL ASSOCIATION, Hollywood, Fla., Dec. 9-11. Dr. John C. Burch, 2112 West End Ave., Nashville 5, Tenn., Secretary.

SOUTHWESTERN MEDICAL ASSOCIATION, Hilton Hotel, Albuquerque, N. M., Oct. 30-Nov. 1. Dr. W. W. Schuessler, 1415 First National Bank Bldg., El Paso, Texas, Secretary.

WESTERN SURGICAL ASSOCIATION, The Shamrock, Houston, Texas, Dec. 4-6. Dr. Michael L. Mason, 154 East Erie St., Chicago 11, Secretary.

INTERNATIONAL

CONGRESS OF INTERNATIONAL LEAGUE AGAINST RHEUMATISM, Geneva and Zurich, Switzerland, Aug. 24-29, 1953. For information write: Dr. W. Tegner, The London Hospital, London E.1, England.

CONGRESS OF THE INTERNATIONAL SOCIETY OF SURGERY, Lisbon, Portugal, Sept. 15-20, 1953. Dr. L. Dejardin, 141, rue Belliard, Brussels, Belgium, General Secretary.

INTER-AMERICAN CONGRESS OF RADIOLOGY, Mexico City, Mexico, Nov. 2-8. Dr. Guido Torres Martinez, Marsella No. 11, Mexico, D.F., Secretary-General.

INTER-AMERICAN SESSION, American College of Surgeons, Paulista Medical Association Bldg., Sao Paulo, Brazil, Feb. 9-12, 1953. Dr. Moacyr Eyck Alvaro, 1151 Conselacao, Sao Paulo, Brazil, Chairman.

INTERNATIONAL CONGRESS OF AUDIOLOGY, Groningen, Netherlands, June 5-6, 1953. Dr. Gunnar Holmgren, Strandvagen 5A, Stockholm, Sweden, President.

INTERNATIONAL CONGRESS OF ELECTROENCEPHALOGRAPHY AND CLINICAL NEUROPHYSIOLOGY, Boston, Mass., U. S. A., Aug. 18-21, 1953. Dr. Robert S. Schwab, Massachusetts General Hospital, Boston 14, Mass., U. S. A., Secretary-General.

INTERNATIONAL CONGRESS FOR HISTORY OF SCIENCE, Jerusalem, Israel, August 3-7, 1953. Prof. F. S. Bodenheimer, Hebrew University, Jerusalem, Israel, President.

INTERNATIONAL CONGRESS ON HYDATID DISEASE, Santiago, Chile, Nov. 21-24. Organizing Committee, P. O. Box 9183, Santiago, Chile.

INTERNATIONAL CONGRESS ON MEDICAL LIBRARIANSHIP, London, England, July 20-25, 1953. Mr. W. R. LeFanu, % London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C.1, England, Chairman.

INTERNATIONAL CONGRESS OF MICROBIOLOGY, Rome, Italy, Sept. 6-12, 1953. For information write: Dr. V. Puntoni, Citta Universitaria, Rome, Italy.

INTERNATIONAL CONGRESS OF MILITARY MEDICINE AND PHARMACY, Montevideo, Uruguay, March 1-7, 1953. Dirreccion General del Servico de Sanitad Militar, 8 de Octubre y Mariano Moreno, Montevideo, Uruguay, Secretariat of the Congress.

INTERNATIONAL CONGRESS OF OTORHINOLARYNGOLOGY, Amsterdam, Netherlands, June 8-15, 1953. Dr. W. H. Struben, J. J. Viottastraat 1, Amsterdam, Netherlands, Secretary.

INTERNATIONAL CONGRESS OF RADIO-BIOLOGY, Copenhagen, Denmark, July 14-25, 1953. Prof. Flemming Norgaard, Oster Voldgade 10, Copenhagen K, Denmark, Secretary General.

INTERNATIONAL CONGRESS OF RADIOLOGY, Copenhagen, Denmark, July 19-25, 1953. Professor Flemming Norgaard, 10 Oster Voldgade, Copenhagen K., Denmark, Secretary General.

INTERNATIONAL CONGRESS OF THALASSOTHERAPY, Dubrovnick, Yugoslavia, May 17-25, 1953. Prof. C. Plavaic, Mavrodne Republick 51, Belgrade, Yugoslavia, Secretary General.

INTERNATIONAL CONGRESSES OF TROPICAL MEDICINE AND MALARIA, Istanbul, Turkey, Aug. 28-Sept. 4, 1953. Professor Dr. Ihsan Sükrü Aksel, Tunel Meydam, Beyeglu, Istanbul, Turkey, General Secretary.

INTERNATIONAL FERTILITY ASSOCIATION, New York, N. Y., U. S. A., May 25-31, 1953. Dr. Abner I. Weisman, 1160 Fifth Avenue, New York 29, N. Y., U. S. A., Associate Secretary General.

INTERNATIONAL HOSPITAL CONGRESS, London, England, May 25-30, 1953. Capt. J. E. Stone, 10 Old Jewry, London, EC2, England, Hon. Secretary.

INTERNATIONAL PHYSIOLOGICAL CONGRESS, Montreal, Canada, Aug. 31-Sept. 4, 1953. Dr. A. S. V. Burgen, Dept. of Physiology, McGill University, Montreal, Canada, Secretary.

INTERNATIONAL STUDY CONFERENCE ON CHILD WELFARE, Bombay, India, Dec. 5-12. For information write: All India Save the Children Committee, 5 Carmichael Road, Bombay, India.

INTERNATIONAL UNION AGAINST CANCER AND INTERNATIONAL CANCER RESEARCH COMMISSION, Joint Meeting, Bombay, India. Dec. 28. Prof. Khanolkar, Tata Memorial Hospital, Bombay, India, President.

INTERNATIONAL VETERINARY CONGRESS, Stockholm, Sweden, Aug. 9-15, 1953. Prof. Axel Isaksson, Institute of Veterinary Medicine, Stockholm 50, Sweden, Secretary.

PAN AMERICAN CONGRESS OF THE MEDICAL PRESS, Buenos Aires, Argentine, July 12-16, 1953. Secretaria del Congress, 763 Uriburu, Buenos Aires, Argentine.

WORLD CONFERENCE ON MEDICAL EDUCATION, British Medical Association House, Tavistock Square, W.C.1, London, England, Aug. 24-29, 1953. Secretariat: World Medical Association, 2 East 103d St., New York 29, N. Y., U. S. A.

WORLD CONGRESS OF THE WORLD CONFEDERATION FOR PHYSICIAL THERAPY, London, England, Sept. 7-12, 1953. Miss M. J. Neilson, Chartered Society of Physiotherapy, Tavistock House, South, Tavistock Square, London, W.C.1, England, Secretary

EXAMINATIONS AND LICENSURE

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: *Part I and II.* February 1953. All centers where there are five or more candidates. Exec. Sec., Dr. John P. Hubbard, 133 South 36th St., Philadelphia 4.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Written.* Various locations, July 17. Final date for filing applications is January 17. Sec., Dr. C. B. Hickcox, 80 Seymour St., Hartford 15.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: *Oral.* Philadelphia, October 1953. Final date for filing application is May 1. Ex. Sec., Miss Janet Newkirk, 66 East 66th St., New York 21.

AMERICAN BOARD OF INTERNAL MEDICINE: *Oral.* Philadelphia, Nov. 13-14 and Washington, D. C., Nov. 17-18. Exec. Sec.-Treas., Dr. William A. Werrell, 1 West Main Street, Madison 3.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: *Oral.* Chicago, May or June 1953. Final date for filing application for the oral examination is Jan. 15, 1953. Sec., Dr. Leonard T. Furlow, Washington University School of Medicine, Kingshighway and Euclid Ave., St. Louis.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Written.* Various Centers, Feb. 6, 1953. Final date for filing applications is Nov. 1. Sec., Dr. R. L. Faulkner, 2105 Adelbert Road, Cleveland 6.

AMERICAN BOARD OF OPHTHALMOLOGY: *Written.* Various Centers, January 1953. Final date for filing applications was July 1. *Practical.* New York City, June 6-10, 1953. Sec., Dr. Edwin B. Dunphy, 56 Ivie Road, Cape Cottage, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: The deadline for the receipt of applications for the 1953 Part II examinations was Aug. 15; for the 1953 Part I examination the deadline is Nov. 30. Sec., Dr. Harold A. Sofield, 122 S. Michigan Ave., Chicago.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Oral.* New Orleans, April 21-25, 1953. Sec., Dr. Dean M. Lierle, University Hospital, Iowa City.

AMERICAN BOARD OF PEDIATRICS: *Oral.* Boston, Dec. 5-7. Exec. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

AMERICAN BOARD OF PHYSICAL MEDICINE AND REHABILITATION. *Oral and Written.* June 1953. Final date for filing applications is March 15. Sec., Dr. Robert L. Bennett, 30 N. Michigan Blvd., Chicago.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New York City, Dec. 15-16. Final date for filing applications was Sept. 15. Sec.-Treas., Dr. David A. Boyd, Jr., 102-110 Second Ave. S.W., Rochester, Minn.

AMERICAN BOARD OF RADIOLOGY: *Oral.* Dec. 1-7. Final date for filing application was June 1. *Oral.* Tampa, April 8-15. Sec., Dr. B. R. Kirklin, 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Written.* Various Centers, March 1953. Final date for filing application is Dec. 1. Sec., Dr. John B. Flick, 225 S. 15th St., Philadelphia.

AMERICAN BOARD OF UROLOGY: *Written.* Various Centers, December. *Oral.* Chicago, Feb. 7-11. Sec., Dr. Harry Culver, 30 Westwood Road, Minneapolis 16, Minn.

DEATHS

Miller, Heymen Rudolph ⊕ New York; born in Russia May 24, 1888; Columbia University College of Physicians and Surgeons, New York, 1911; at one time on the faculty of his alma mater; an associate and assistant professor of medicine, New York Post-Graduate Medical School and Hospital, 1925-1926; during World War II chief of the climatic research laboratory of the signal corps at Fort Monmouth, N. J.; associate attending physician at Montefiore Hospital; author of "Angina Pectoris: Nerve Pathways, Physiology, Symptomatology and Treatment," "Angina Pectoris and Myocardial Infarction: With Special Reference to the Autonomic Nervous System," and "Central Autonomic Regulations in Health and Disease"; died in Pound Ridge, N. Y., Aug. 23, aged 64, of coronary occlusion.

Schoenbach, Emanuel Barnett ⊕ Brooklyn; born in New York City Nov. 11, 1911; Harvard Medical School, Boston, 1937; professor of medicine at the State University of New York, College of Medicine at New York City; at one time on the faculty of his alma mater and Johns Hopkins University School of Medicine in Baltimore; certified by the National Board of Medical Examiners; specialist certified by the American Board of Internal Medicine; member of the American Society for Clinical Investigation; served during World War II; director of medical services at Maimonides Hospital; editor in chief, *Quarterly Review of Medicine;* died Sept. 6, aged 40, of coronary thrombosis.

Chase, E. Frank ⊕ Seattle; University of Minnesota College of Medicine and Surgery, Minneapolis, 1905; an Associate Fellow of the American Medical Association; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology and Pacific Coast Oto-Ophthalmological Society; fellow of the American College of Surgeons; affiliated with Children's Orthopedic and Providence hospitals; died in the Virginia Mason Hospital Aug. 4, aged 73, of pulmonary edema, cerebrovascular hemorrhage, and hypertension.

Adams, Frank Mears ⊕ Providence, R. I.; born Jan. 20, 1881; Yale University School of Medicine, New Haven, 1906; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology, American Laryngological, Rhinological and Otological Society, and New England Otolaryngological Society; affiliated with Westerly (R. I.) Hospital, Butler Hospital, Charles V. Chapin Hospital, and the Rhode Island Hospital, where he died Aug. 28, aged 71, of nephrosclerosis and hypertensive cardiovascular disease.

Anderson, David Derricks ⊕ Minneapolis; University of Minnesota Medical School, Minneapolis, 1920; member of the American Academy of General Practice; died in the Swedish Hospital July 31, aged 62, of complications following surgery for strangulated hernia.

Andrews, Malcolm Percival ⊕ Manitowoc, Wis.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1905; member of the American Academy of Ophthalmology and Otolaryngology; died July 29, aged 73, of coronary occlusion.

Cain, Norman Hugh, Atlanta, Ga.; Jefferson Medical College of Philadelphia, 1922; formerly assistant medical director of the Travelers Life Insurance Company of New York; died in Piedmont Hospital July 18, aged 55, of rheumatic heart disease with mitral stenosis.

Campbell, James Alonzo ⊕ Dothan, Ala.; University of Oklahoma School of Medicine, Oklahoma City, 1915; served during World War I; affiliated with Frasier-Ellis and Moody hospitals; died in Saluda, N. C., July 28, aged 63, of coronary thrombosis.

⊕ Indicates Member of the American Medical Association.

Carmody, Thomas James ⊕ Hollywood, Fla.; St. Louis University School of Medicine, 1907; specialist certified by the American Board of Otolaryngology; member of the Illinois State Medical Society; formerly practiced in Danville, Ill., where he was affiliated with Lake View and St. Elizabeth hospitals; died in Veterans Administration Hospital in Hines, Ill., July 27, aged 68, of bronchogenic carcinoma with metastases.

Carruth, Walter Evereth ⊕ Brownsville, Texas; Memphis (Tenn.) Hospital Medical College, 1890; at one time practiced in Corpus Christi, where he was city and county health officer; died May 5, aged 92.

Cohen, Joseph Powitzer, Framington, Mass.; Harvard Medical School, Boston, 1914; fellow of the American College of Surgeons; formerly professor of clinical gynecology at Tufts College Medical School, Boston, and instructor in obstetrics at Harvard Medical School; served during World War II; for many years affiliated with Boston City Hospital and Beth Israel Hospital in Boston; until recently on the staff of the Cushing Veterans Administration Hospital; died Aug. 13, aged 64, of heart disease.

Coulter, Wilbur Edwin ⊕ Seneca, Ill.; Northwestern University Medical School, Chicago, 1910; president of the school board; affiliated with Ryburn Memorial Hospital in Ottawa; director of the Community Bank; died in Martinsville, Va., July 25, aged 68, of coronary disease.

Dalton, James Breckenridge ⊕ Richmond, Va.; University College of Medicine, Richmond, 1910; member of the American Academy of Orthopaedic Surgeons; past president of the Virginia Orthopedic Society; affiliated with Retreat for the Sick, Stuart Circle Hospital, and the Medical College of Virginia Hospital Division; died July 14, aged 66, of nephritis, hypertension, and cerebral hemorrhage.

Davis, Charles E. ⊕ Linden, Texas; Memphis (Tenn.) Hospital Medical College, 1901; for three years president of the school board; served as president of the Cass-Marion Counties Medical Society; died recently, aged 83, of cerebral hemorrhage.

Davis, Murray Bell ⊕ Nashville, Tenn.; Vanderbilt University School of Medicine, Nashville, 1918; fellow of the American College of Surgeons; formerly on the faculty of Meharry Medical College; affiliated with Nashville General, Protestant, and St. Thomas hospitals; died July 22, aged 58, of a heart attack.

Drew, Charles Aaron ⊕ Worcester, Mass.; University of Vermont College of Medicine, Burlington, 1884; member of the New England Society of Psychiatry; formerly assistant physician at Taunton (Mass.) State Hospital, assistant superintendent, Medfield (Mass.) State Hospital, director, Bridgewater State Hospital in State Farm, and superintendent Worcester City Hospital, where he died July 9, aged 93, of carcinoma of the prostate.

Dysart, Benjamin Quincy ⊕ Henry, Ill.; University of Illinois College of Medicine, Chicago, 1918; past president of the Bureau County Medical Society; affiliated with St. Margaret's Hospital; surgeon for the Rock Island Railroad; died in Yakima, Wash., July 29, aged 59, of acute hemorrhagic pancreatitis.

Frank, Myrtile ⊕ Egg Harbor City, N. J.; University of Tennessee Medical Department, Nashville, 1900; mayor of Egg Harbor from 1930 to 1936; since 1945 medical inspector for the Egg Harbor schools; since 1924 president of the board of health; affiliated with Atlantic City (N. J.) Hospital, where he died July 1, aged 75, of endarteritis obliterans.

Gillespie, Chauncey Marshall, Medaryville, Ind.; Bennett Medical College, Chicago, 1910; died in Memorial Hospital, South Bend, July 29, aged 73, of cerebral hemorrhage and hypertension.

Giordano, Anthony Mariano ⊕ Reading, Pa.; Georgetown University School of Medicine, Washington, D. C., 1935; served during World War II; affiliated with St. Joseph's Hospital, where he died July 19, aged 44, of Hodgkin's disease.

Griffith, Joseph Kimberlin ✠ Robert Lee, Texas; Kansas City (Mo.) Medical College, 1891; also a graduate in dentistry; formerly county health officer; died recently, aged 86, of coronary sclerosis.

Hascall, Theodore Conrad ✠ Riverside, R. I.; Cornell University Medical College, New York, 1909; served during World War I; school physician; affiliated with the Memorial Hospital in Pawtucket; died July 27, aged 68, of cerebral hemorrhage.

Hersey, Fred D., Casnovia, Mich.; Physio-Medical College of Indiana, Indianapolis, 1894; died July 15, aged 85, of coronary occlusion.

Hill, William Everett ✠ Cleveland; Western Reserve University School of Medicine, Cleveland, 1922; served during World War I; on the staff of the Glenville Hospital; died in Hanna House of University hospitals July 29, aged 62, of myocardial infarction.

Hinkley, Frederick Josiah, Stanberry, Mo.; Barnes Medical College, St. Louis, 1901; died in St. Joseph (Mo.) Hospital July 26, aged 72, of chronic myocarditis.

Hughes, Singleton Bernard, Baltimore; Howard University College of Medicine, Washington, D. C., 1905; for many years on the staff of the Provident Hospital; died in Johns Hopkins Hospital July 23, aged 73, of squamous cell carcinoma of the mouth.

Johnson, Milton John ✠ Jamestown, N. Y.; Cornell University Medical College, New York, 1906; fellow of the American College of Surgeons; affiliated with Jamestown General and Woman's Christian Association hospitals; died July 30, aged 70, of pulmonary tuberculosis.

Johnson, Oscar Victor, Springfield, Ohio; University of Minnesota College of Medicine and Surgery, Minneapolis, 1905; died July 24, aged 74, of cerebral embolism.

Jungman, John Drummond, Philadelphia; University of the South Medical Department, Sewanee, Tenn., 1906; member of the American Public Health Association; at one time epidemiologist in the Philippine Islands; formerly associated with the U. S. Public Health Service; served during World War I; examiner for the Veterans Administration at the time of his death July 24, aged 66, of cardiac failure.

Kermisch, Albert, Baltimore; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1931; died June 24, aged 45, of cerebrovascular accident.

Kliatshco, Mark Gordon ✠ Mount Vernon, N. Y.; University of Michigan Medical School, Ann Arbor, 1924; affiliated with Mount Vernon Hospital, where he died July 23, aged 50, of cerebrovascular accident.

Merrick, Edward H. ✠ San Antonio, Texas (licensed in Texas under the Act of 1907); died June 11, aged 67, of heart failure.

O'Brien, John Daniel ✠ Canton, Ohio; Jefferson Medical College of Philadelphia, 1903; member of the American Psychiatric Association and the Central Neuropsychiatric Association; served during World War I; affiliated with Mercy Hospital; died July 16, aged 71, of coronary occlusion.

O'Connell, John C. ✠ Rantoul, Ill.; Chicago College of Medicine and Surgery, 1914; served during World War I; acting health officer of Rantoul for 28 years; affiliated with Mercy Hospital in Urbana; died July 11, aged 63, of coronary occlusion.

Osborne, LeRoy Jakway ✠ Owego, N. Y.; University of Buffalo School of Medicine, 1913; member of the American Academy of Pediatrics; died July 14, aged 61, of acute coronary thrombosis.

Perreault, Raymond Richard ✠ Rochester, N. H.; McGill University Faculty of Medicine, Montreal, Canada, 1935; fellow of the American College of Surgeons; affiliated with Frisbie Memorial Hospital; died in Alton July 27, aged 43, of accidental drowning.

Pettit, George Dewey, Chilhowie, Va.; Medical College of Virginia, Richmond, 1929; died June 20, aged 54.

Pope, Frank William, Louisville, Ky.; Louisville National Medical College, Medical Department State University, 1912; died in the General Hospital July 6, aged 66, of coronary occlusion.

Rood, George L. ✠ Ithaca, N. Y.; Eclectic Medical Institute, Cincinnati, 1883; died July 25, aged 97, of arteriosclerosis and prostatitis.

Rosenberg, Martin J. ✠ New York City; Universität Heidelberg Medizinische Fakultät, Baden, Germany, 1914; died June 21, aged 61, of coronary sclerosis.

Ryan, Granville Nimrod ✠ Franklin, Mich.; Rush Medical College, Chicago, 1895; member and formerly vice-president of the Iowa State Medical Society; past president of the Polk County (Ia.) Medical Society; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; died in St. Joseph's Hospital, Pontiac, July 18, aged 82, of cerebral hemorrhage.

Senerchia, Giovanni ✠ West Warwick, R. I.; Regia Universita di Napoli Faculta di Medicina e Chirurgia, Italy, 1915; served with the Italian Army during World War I and received the War Cross from the Ministry of War; past president of the Kent County Medical Society; medical examiner for the Selective Service System, Kent County board no. 2 from 1940 to 1944 and from 1946 to 1952; on the staff of St. Joseph's Hospital in Providence; died Aug. 16, aged 69, of carcinoma of the tongue.

Shell, William Thomas ✠ Corsicana, Texas; Atlanta Medical College, 1895; fellow of the American College of Surgeons; past president and secretary-treasurer of the Navarro County Medical Society; formerly city health officer; affiliated with Corsicana and Physicians and Surgeons hospitals; died July 3, aged 78.

Sloterbeck, Edgar Blackburn ✠ Monessen, Pa.; Jefferson Medical College of Philadelphia, 1907; served during World War I; died July 30, aged 70.

Sperry, Herbert Edgar, Coral Gables, Fla.; Albany (N. Y.) Medical College, 1908; served during World War I; died in Miami July 6, aged 69, of rupture of the aorta.

Staub, Richard John, Elba, N. Y.; University of Buffalo School of Medicine, 1907; died July 16, of cerebral hemorrhage and arteriosclerosis.

Stevens, Thomas F. A. ✠ Baltimore; University of Maryland School of Medicine, Baltimore, 1912; died in St. Joseph Hospital July 26, aged 66, of thrombosis of the inferior mesenteric artery, cardiac decompensation, and diabetes mellitus.

Stollenwerck, Amasa Dorman ✠ Jacksonville, Fla.; Medical Department of Tulane University of Louisiana, New Orleans, 1908; fellow of the American College of Surgeons; affiliated with Duval Medical Center and St. Vincent's Hospital, where he died July 29, aged 67, of arteriosclerotic heart disease.

Vanorden, Herbert Francis ✠ Kansas City, Mo.; Johns Hopkins University School of Medicine, Baltimore, 1910; emeritus professor of obstetrics and gynecology at the University of Kansas School of Medicine; an Associate Fellow of the American Medical Association; member of the Central Association of Obstetricians and Gynecologists; fellow of the American College of Surgeons; affiliated with St. Mary's and Research hospitals; died July 29, aged 68, of acute coronary occlusion.

Walker, Thomas Duhart, Denbigh, Va.; University of Louisville (Ky.) Medical Department, 1909; served as medical director of the Patrick Henry Hospital; for a time city physician of Newport News; died July 27, aged 68.

Wallgren, Andrew Bennett, Pittsburgh; Western University of Pennsylvania Medical Department, Pittsburgh, 1902; on the faculty of the University of Pittsburgh until 1945; died June 8, aged 74, of cardiovascular renal disease.

Wehmeyer, Eugene, Campbell Hall, N. Y.; Regia Università di Torino Facoltà di Medicina e Chirurgia, Italy, 1900; died July 2, aged 76, of pernicious anemia and arteriosclerosis.

Wiggins, George ✠ New Castle, Ind.; St. Louis University School of Medicine, 1931; died May 16, aged 48, of coronary occlusion and chronic hepatitis.

Witten, Paul ✠ San Fernando, Calif.; Northwestern University Medical School, Chicago, 1937; served during World War II; died in San Fernando Hospital Aug. 1, aged 42, of nephritis following an appendectomy.

FOREIGN LETTERS

CHILE

Amebiasis in Childhood.—Drs. R. Ortega and H. Suarez, of the pediatric section of the Clinical Hospital of Concepcion, presented a study made among hospitalized children suffering from diarrheal syndrome. In 54 cases clinical amebiasis was suspected. Of these, 90% had a positive parasitological stool examination for Endamoeba histolytica and a positive rectoscopy. Nine per cent had a positive rectoscopy and a negative parasitological test. Of the 54 patients, 95% were less than 2½ years old and only 3 were between 3 and 8 years of age. This greater percentage of infants could be due to the fact that diarrhea affects the infant more deeply and seriously than it does the older child, thus forcing the hospitalization of the infant whereas the older child is generally ambulatory. It must be noted that 66% of the patients are less than 9 months of age. The dysenteric syndrome was present in the great majority of cases and was the reason for hospitalization. There was no appreciable difference in sex noted. The possibility of family contagiousness was investigated in 19 cases, and in all these cases at least one member of the family suffered from amebiasis. It seems that there is a predominance of the infection in the summer months. Of the 54 children, only 1 was breast-fed and 53 had artificial food (cow's milk or canned products). Only 15% of the children could be classified as eutrophic, the rest being dystrophic. The reason for the first consultation in 82% of the cases was diarrhea. In the history special attention was given to previous episodes of diarrhea. In 48% of the patients the diarrhea episode was less than a month old. Periods of diarrhea that alternated with periods of well-being were highly suggestive of amebiasis. Regarding the aspect of the stools, in 82% it had a frankly dysenteric aspect (blood, pus, and mucus), in 9% it had only mucus and was semiliquid, and in 9% it was normal.

A great majority of the infants had a bad nutritional condition because of chronic diarrhea, an alimentary deficiency, or both. The general well-being of the patient was seriously affected, especially if one considers that 33 out of the 54 cases occurred in spring or summer, months of great dehydration. Approximately 70% of the patients were in serious danger, 18.5% of them having toxicosis. Abdominal pain was one of the most constant symptoms during the acute stage of amebiasis in childhood. Fever was present in all the cases at some time during the disease; however, it is impossible to describe a typical amebic fever in infants either because they presented simultaneously another type of infection or because they were very dehydrated. Hepatomegaly was more frequent than splenomegaly. The concomitant diseases were, generally speaking, those of a dystrophic child: otitis, bronchopneumonia, and pyuria. Regarding the laboratory tests, a hypochromic anemia was generally present. A leukocytic count of over 10,000 was found in more than 70% of the cases. In 23% an eosinophilic count of more than 6% was present. It is difficult to consider the number of days of hospitalization because these patients, besides suffering from amebiasis, were treated for their dystrophic condition. Eight infants died, but the cause of death was not always amebiasis. Amebiasis was directly responsible in three cases, and in the other five it was a factor that greatly contributed to death.

Rectosigmoidoscopy was performed by Dr. C. Treur and proved to be an excellent complementary method of diagnosis of amebiasis in children, reaching up to 76% of positivity. In 36 cases the rectosigmoidoscopic evolution of the lesions was made. In these in 26 cases the first sign of healing was the disappearance of amebas from the stool, and in 6 cases it was the correction of the rectoscopic image that was first observed. In the remaining four cases it was the variation of the characters of the stool that was the first sign of healing.

The first sign of improvement is the occurrence of negative results in the stool examinations; then comes clinical improvement, and last comes the anatomic reconstitution. When results of endoscopy are normal, the patient can be considered cured. The clinical improvement is not a good criterion on which to base the cure of amebiasis; because of the frequency of spontaneous remissions of the diarrhea. Rectoscopy together with a persistent negative stool examination is a much better guide.

Regarding the treatment, emetine hydrochloride was used with great caution and only to counteract tenesmus. A dosage of 50 mg. per day was used and never for more than three to four days. No opinion can be formed regarding the effects of pentavalent arsenical products (carbarsone) because they were always used as complements. When diiodohydroxyquinoline was used, a low percentage (25%) of good results was obtained in 20 cases even when doses as high as 100 mg. per kilogram of body weight for periods as long as 20 days were administered. Therefore its use should be limited to cases in which other drugs have failed. Aureomycin was used in 12 cases, with good results in 83%. Adequate doses seem to be 50 to 100 mg. per kilogram daily for 10 to 15 days. Terramycin in similar dosification did not prove to be equally efficacious, but owing to the fact that only seven cases were treated no definite opinion can be formulated.

Cephalalgia and Hypertension.—Recently Drs. R. Guzman and H. Serani of the clinic of Prof. Armas-Cruz studied 400 patients suffering from high blood pressure and compared them with a control group of 400 persons. In order to eliminate all possible cases of arteriosclerosis, persons over 60 years of age were eliminated from the study. In special questionnaires the patients reported their age, sex, blood pressure, presence of headache and its characteristics, date of its existence, therapy used, and its results. Patients who knew that they had high blood pressure were separated from those who did not know that they were suffering from hypertension; this was done mainly to investigate the action of the psychological factor. In patients suffering from high blood pressure, 42% presented cephalalgia compared with 20% in the group of persons with normal blood pressure. Cephalalgia is present twice as often in women suffering from high blood pressure as in men (64% as compared with 32%). A point of interest is that headache was present twice as often in the group that knew that they had high blood pressure as in the group that did not know. In the latter group the frequency of the symptom was 27%, that is, practically as frequent as in the normal blood pressure group. The authors observed that the values of the blood pressure only moderately influenced the presence of cephalalgia. In the majority of cases the headache was localized in the frontal region and appeared generally in the morning. Analyzing the pathogenesis of cephalalgia in hypertension the authors believe that it is due to vasodilatation and to a greater pulsatility of the branches of the external carotid. The importance of psychogenic factors in the appearance of cephalalgia is emphasized. Summarizing the treatment, the authors give great importance to psychotherapy and the use of vasoconstricting drugs (ergotamine and caffeine) and sedatives during the pain periods.

Classification of Anemias.—Rodolfo Armas-Cruz, professor of medicine of the University of Chile, recently proposed the following new classification of anemias partially based on the division of jaundice into premedullary anemias (prehepatic jaundice), medullary anemias (hepatic jaundice), postmedullary anemias (posthepatic jaundice), and finally anemias of uncertain causation (secondary anemias). The classification has the advantage of being extremely didactic, physiopathological, and morphological simultaneously.

Premedullary anemias are represented by the anemias in which there is a failure of a substance necessary for the maturation of the red blood cell. The most important anemias of this

The items in these letters are contributed by regular correspondents in the various foreign countries.

group are iron deficiency anemias, vitamin B deficiency anemias (including vitamin B_{12} and folic acid [Lactobacillus casei] deficiency anemias, and hormonal failure anemias [including hypothyroidism anemia]). Medullary anemias are those in which there is a decreased amount or atrophy of the bone marrow tissue or there is a substitution by other tissue (myelopathic anemias) either from outside the bone marrow (cancer metastasis and lymphosarcoma) or from the pathological hyperplasia of one of the normal elements of the bone marrow (leukemia). Postmedullary anemias are represented by posthemorrhagic anemias and hemolytic anemias. In these three groups two types of anemias are not taken into consideration: the so-called secondary anemias, produced by a deficiency in production of red blood cells or of the bone marrow itself and a peripheral disturbance; and hypersplenism anemias, whose origins probably are medullary but might involve other mechanisms sometimes connected with hemolysis.

Epidemiology of Amebiasis.—Drs. Neghme and Silva reported the results of a coprological study made of 8,390 persons in 46 different localities between the years 1948 and 1951. Preference was given to those living in rural and suburban sectors; no selection regarding age or sex was made. The authors studied the geographic distribution of enteroparasitosis in Chile in relation to the great topographic and climatic differences of the various regions of the country. Whereas the frequency of amebiasis is high in all three zones (north, central, and south) and the infection attacks mainly the adolescent and adult group, other forms of enteroparasitosis are more frequent in infancy and in the younger age group. Regarding their geographic distribution, Giardia lamblia is more frequent in the north of the country and Ascaris lumbricoides and Trichuris trichiura are more frequent in the south where the climate is colder and damper. Of the 8,390 persons examined, 1,980 presented evidence of Endamoeba histolytica. In certain parts of the south of Chile as many as 65% of the persons examined were infected with A. lumbricoides and T. trichiura.

SWEDEN

Influence of Measles on Fetal Life.—In 1941 Gregg reported that an attack of measles early in pregnancy is often followed by deafness, diseases of the eye and heart, mental defects, and other developmental anomalies in the mother's offspring. As a result, in Sweden, in 1951 alone, as many as 275 women underwent legally permitted abortions on the plea that Gregg's syndrome was likely to develop in their offspring. The expectant mother needs only to declare in writing that she suffered from measles at any time during her pregnancy to induce the authorities to give the necessary permission for a legal abortion.

At a meeting early in 1952 of the Swedish Medical Society, one speaker suggested that certain women had exploited this loophole in the regulations without having to present a physician's certificate stating that they had actually suffered from measles during their pregnancy. At the same meeting Dr. Rolf Lundström presented a statistical analysis concerning the actual risk of the child's developing Gregg's syndrome in such instances. This analysis was undertaken in connection with a severe epidemic of measles in Sweden culminating from March to May, 1951. Among approximately 45,000 women undergoing spontaneous abortion or confinement in hospital, there were 1,035 who stated that they had suffered from measles during their last pregnancies. Among these were 527 whose attack of measles had occurred during the first four months of pregnancy. Compared with these 527 women were 2,192 women who, not having suffered from measles during pregnancy, served as controls. In the following analysis, the figures in brackets concern the controls. Stillbirths accounted for 2.7% (1.4%) of the 527 measles cases, congenital debility for 8.3% (2.5%), and malformations for 6.6% (1.2%). Altogether, 93, or 17.6%, of the 527 cases presented one or another of these three conditions, whereas the corresponding figure for the controls was much smaller (5.1%). Also all the ill-effects due to measles did not appear at once, and mental deficiency due to it sometimes did not become evident before school age was reached.

At the same meeting figures that showed a different conclusion were presented by Dr. J. A. Abolins who gave an analysis of the hospital records of some 28,000 expectant mothers in 1950-1951. They were asked if they had suffered from measles in childhood or later on. If measles had coincided with pregnancy, they were asked at what stage of it the infection had occurred. About 1% of the women had suffered from measles during their pregnancy, and in a few of these cases the offspring had shown some anomaly or other. But there was not one case in which Gregg's syndrome could be linked up with measles in the mother during her pregnancy. Dr. Abolins said that in his opinion there was neither a medical nor eugenic indication for inducing abortion for this reason, and he remarked that Sweden is the only country in the world in which abortion is induced so often on this count.

Meanwhile, systematic investigations continue to be pursued in Sweden in order to throw more light on the matter, and at the Södersjukhuset a special study is being undertaken of the eyes of those infants whose mothers suffered from measles. These studies were started in September, 1951, and among the first 1,500 infants examined were 13 whose mothers had suffered from measles between the second and the seventh months of pregnancy. The problem is still to be investigated, and one of the difficulties involved is that measles is sometimes difficult to diagnose with certainty.

Free School Breakfasts.—For many years the school children of Stockholm have been given free breakfasts when their parents could show that the children were in real need of them. In 1946 the Swedish Parliament went a step further, decreeing that every school child should be eligible for a free breakfast, for which the local and social authorities were to pay. There was, however, to be a provisional means test for the first five years, while this system was being organized and the necessary buildings were being erected. This provisional arrangement is still in force, as the organization and building took longer than was expected. By 1951-1952 approximately 90% of all the school children in Stockholm were in receipt of free breakfasts at a cost of 80 öre per head per breakfast and about 10 million kroner per year.

A school medical officer, Dr. Per J. Nordenfelt, discussed both sides of the situation in the organ of the Swedish Medical Association, *Svenska läkartidningen* for Aug. 1, 1952. Among the favorable points is the assurance that every child can, at least once a day, be supplied with a well-balanced meal at which a high dietetic standard is set. The child who is overly fastidious about his food at home learns from his schoolfellows to better appreciate his food. A sense of comradeship and solidarity is also created as the children eat together, and the mothers are free at home to attend to duties other than cooking. There is also the economy effected, and this may be appreciable in large families. On the other hand, these free breakfasts require new buildings erected at the expense of other houses much needed in the present housing crisis. The staff needed to cook and serve the breakfasts might otherwise have been employed in nursing the sick and aged. Collective breakfasts also mean the loss to the child of the educational benefits of eating at home with its parents, just one more step toward separating the child from his parents. For many children, the younger in particular, it is a severe strain to remain uninterruptedly away from home from 8 a. m. till 4 p. m. Then there are the sensitive children for whom it is a severe ordeal to enter a large room in which 300 to 400 children are eating at the same time. There are also the children who require special diets.

The greatest difficulty arising in connection with these collective meals concerns the interval between eating and the return to lessons. When the distance between school and home is short, this interval can be filled by returning to the home, but it is difficult to place and employ the other children satisfactorily during this interval. Dr. Nordenfelt's personal opinion on the matter is that it would have been better if the evolution of the free school breakfast had been allowed to proceed more gradually, and he would like to emphasize the voluntary aspect of the system so that the free breakfasts could be accepted or refused according to individual needs. The most satisfactory arrangement might well be the participation in this system of only 40 to 60% of all the children, the other 40 to 60% being allowed to eat their breakfast at home without any social pressure being applied.

CORRESPONDENCE

AN ILEOSTOMY CLUB

To the Editor:—In recent years heightened interest in the surgical treatment of ulcerative colitis has led to an ever-increasing group of patients with a permanent ileostomy. Most lay persons, as well as all too many physicians and surgeons, have a horror image of the constantly discharging intestinal stoma and frequently think, out of ignorance, that death is preferable to ileostomy. It is therefore extremely important for the person who has undergone ileostomy to have before him the evidence that adjustment can be made and the constant reminder that he is not so unfortunate as he might have imagined. Nothing is more effective in bolstering morale than the presence of happy persons with the same handicap carrying on normal existence, unabashedly attacking the specific problems that the handicap may cause.

During the past one and one-half years at the Mt. Sinai Hospital we have had a club meeting once a month that was attended by patients who have had ileostomy for the treatment of ulcerative colitis on the ward surgical service. Patients from other services and other hospitals have learned of meetings and keep coming in increasing numbers. These meetings have been so well attended, active, and educational that such an organization could serve as a pattern for other groups throughout the country to follow.

The present organization shows little resemblance to the first small social gathering at the home of one of the eight girls who had come to know each other on the wards at the hospital. Yet it was this spontaneous effort that was to lead to the larger grouping. Miss L. M. Neary, social worker on the surgical wards, and I traveled out to the second gathering, attended this time by only five of the original eight. It was clear to us that these few patients had a most valuable idea, which needed only nurturing. In the subsequent months, therefore, notices were sent to most of the former patients who had undergone ileostomy, arrangements were made for room space at the hospital, meetings were scheduled regularly, refreshments were added, and various medical subjects were discussed. At the end of the meeting, mechanical problems of a few were managed individually. In a short time, the club grew rapidly. Members who attended the monthly meetings sometimes regularly traveled from long distances in inclement weather. A constitution was drawn, officers were elected, and dues were established. The first small room has given way to a larger, more convenient room, and arrangements are now being made for still larger space.

There are now 50 active members and 5 officers established by the constitution and elected by the members. The meetings are held regularly every month in a lounge at the hospital. Postoperative patients are wheeled from the wards to attend, and in a few instances patients for whom ileostomy had been decided on and scheduled have been brought in. A mimeographed newspaper is printed by the members and distributed at each meeting. It contains news and gossip of the activities of the members, medical information, abstracts of talks given at the meetings, information about purchase of paste and other materials, and humorous articles relating to the hospitals, nurses, and doctors. The agenda is planned in advance.

In the past year the club tried and settled on various types of chlorophyll tablets for oral administration, and ileostomy appliances of several companies were tested by volunteer members and reported on in detail. Each of the patients on the ward who has recently undergone ileostomy is visited by a club member, who gives advice and encouragement on ileostomy management. Medical guests, usually from the staff, are invited to the meetings to give brief talks and answer questions. A staff psychiatrist has addressed the group and now attends the meetings regularly but principally as an observer rather than as a participant. Discussions are usually extremely lively and interesting. After the business meeting, refreshments are served and a general social mingling occurs. The club is named "QT Alumni," after the two wards. By chance, the slang meaning of "keeping quiet" is also conveyed by the QT letters, but there is nothing secret about the club in the hospital. The only secrecy extends to keeping the neighbors of each member from knowing about his ileostomy.

In the process of the club's development several lessons have been learned that should be passed on to those who may seek to establish similar groups elsewhere. There should be a regular place, date, and time for each meeting, so that members can plan to be free for attendance. In addition, cards announcing the meeting should be sent to the members about a week before. The meetings, election, organization, and decisions should be in the hands of the members rather than the medical personnel. It is, however, of great importance to have someone from the attending staff who will act as sponsor and who will advise, attend all meetings, stimulate activity, and be available for consultations regarding club business; yet he must be prepared to take a "back seat," allowing the members themselves to run the club. Another essential is a close relationship with the social service department, preferably by having one person who is permanently assigned and who will be the focal point on whom patients, doctors, and hospital administration can converge. At least several days before each meeting, the chairman, together with the officers, should decide on an agenda.

The benefits derived from the "QT Alumni" may be classified as psychological, medical, and educational. The club is an effective means of group psychotherapy. Patients who have recently undergone ileostomy have been able to see many persons like themselves actively engaged in the daily routines of living. Those who have early mechanical problems have learned that others with similar difficulties have conquered them completely. Patients have frequently said that their entire attitudes changed on being visited on the ward by a club member. Some who have been unable or reluctant to manage their appliances properly after leaving the hospital have turned from resentment to cheerful acceptance. Moreover, even the well-adjusted person of long-standing club membership has found an added meaning to his life by serving as an "expert" to help the neophytes along.

Several of the members who have married in the past year have stated that they would not have been able to approach the idea without the support and practical advice they received at the club meetings from members and the medical personnel. The first pregnancy was followed eagerly by the entire club, and soon after the successful and uneventful delivery, several other regular members became pregnant. Recently engaged or newly married members have sometimes come to meetings with their partners. The result has been a reassurance that the person who has undergone ileostomy can and does lead a normal existence.

The medical benefits to the patient are important, in that the problems of an ileostomy are considered and solved in a general way. The best bags, paste, cleansing methods, and deodorants are discussed. Even specific difficulties have been successfully resolved in open meetings. But the attempt to consider each person's management problem at a club meeting was abandoned early, for too much time was needed, the socially beneficial nature of the meeting was diluted, and the specific difficulty often had no bearing on those of the others. For each person's specific needs, a special clinic devoted to intestinal stomas of all types has been established recently at the hospital.

Finally, the club has educated the entire hospital personnel (doctors, nurses, social workers) in the best methods of managing the ileostomy. Doctors who have attended as guests have been astounded by the degree of adjustment achieved by the members. No doctor leaves the meetings without a clearer evaluation of the problems engendered by the ileostomy, a renewed interest in the disease ulcerative colitis, and a more hopeful outlook on the way of life of the patient with an ileostomy.

Furthermore, improvements in appliances have been suggested to the manufacturing companies. Perhaps the most important of all the results achieved by the club has been its demonstration by living example that the patient with an ileostomy can lead a healthy, happy life filled with all the joys and activities of the "normal" persons around him.

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New York 28.

ISONIAZID AND IPRONIAZID RESISTANCE IN PULMONARY TUBERCULOSIS

To the Editor:—As a result of the recent availability, commercially, of isoniazid (isonicotinic acid hydrazid), its use has become widespread in tuberculosis institutions and in the hands of private practitioners. In too many instances, it seems to us, this usage has been rather indiscriminate, based on a few overly enthusiastic medical reports, much premature lay publicity, and without regard to the proper place of this drug in the over-all long-term treatment program. In particular, there has been a scarcity of reports concerning the incidence of isoniazid-resistant strains of tubercle bacilli occurring during isoniazid therapy, the time during continuous therapy when resistance is most likely to occur, and the effect of concomitant administration of *p*-aminosalicylic acid or streptomycin on the development of resistance. Physicians treating tuberculous patients are well aware of the inherent dangers of injudicious use of the various types of antituberculosis therapy and all too often see patients whose chances of eventual recovery have been ruined by poor planning and timing in the use of the antituberculosis drugs, particularly in relation to chest surgery. Since isoniazid is now being used in patients with less severe tuberculosis, many of whom are already resistant to streptomycin, and often in lieu of previously contemplated surgery, the above-mentioned considerations become all the more important. We have recently completed a series of isoniazid and iproniazid sensitivity tests, the results of which will be briefly reported here and in greater detail elsewhere.

Sputum concentrates were planted directly on modified Löwenstein's medium to which isoniazid was added to give final concentrations of 3, 10, and 20 μg per milliliter. Iproniazid ("marsilid") was incorporated in the medium to give final concentrations of 5, 10 and 25 μg per milliliter. Control tubes of the medium without the drug were planted, and tests were discarded in those with negative cultures.

Forty separate sensitivity tests were performed in this manner in 36 patients with far-advanced cavitary pulmonary tuberculosis. Thirty-two of the patients received isoniazid in doses of 5 mg. per kilogram of body weight per day. In four of these the cultures were negative after eight weeks and so were not counted. All the others had positive cultures. Twenty-two patients showed bacterial resistance to the drug in all the concentrations used, the time interval between the beginning of drug administration and sensitivity testing ranging from 7 to 13 weeks. Only six patients manifested sensitivity to the drug after 7 to 11 weeks of administration. Four patients who had received iproniazid ("marsilid") in a dosage of 3 to 5 mg. per kilogram of body weight a day for a six week period were studied. Cultures made from three of these patients showed resistance in concentrations up to 25 μg per milliliter; cultures from the fourth patient showed sensitivity at the end of this period. Because of increasing edema and nitrogen retention, iproniazid therapy was discontinued in these four patients and isoniazid therapy instituted. One patient sensitive to iproniazid and one resistant to this drug were found to be isoniazid resistant after four weeks of isoniazid therapy. Two patients resistant to iproniazid were found to be isoniazid resistant at the start of isoniazid therapy.

In regard to the effect of *p*-aminosalicylic acid or streptomycin on the emergence of isoniazid and iproniazid resistant strains, 14 of 18 patients receiving *p*-aminosalicylic acid concomitantly and 3 of 5 patients receiving streptomycin concomitantly manifested resistance. Two patients receiving both streptomycin and *p*-aminosalicylic acid in addition to isoniazid both showed resistance at the end of 9 and 12 weeks of therapy respectively.

Almost all our patients manifesting bacterial resistance to these drugs have now suffered bacteriological and clinical relapses. We have noted both subjective and objective improvement, often dramatic, occurring within the first month of therapy. Sputum conversions have been frequent, exudates have cleared, and cavities have become definitely smaller but have not entirely closed. Then for the next 6 to 10 weeks there is little or no subjective or objective improvement, and in a few cases the disease has become severer.

We are now investigating intermittent administration of isoniazid (giving 6-8 mg. per kilogram of body weight every third day) in combination with *p*-aminosalicylic acid in the hope that the long-term effect will be beneficial and that emergence of resistant strains will be delayed. From the results of our studies, it is our present opinion that isoniazid should be administered to patients with pulmonary tuberculosis on a short-term basis and as an "umbrella" for surgery, particularly in those patients already streptomycin resistant. Except in tuberculous meningitis, in which we have found isoniazid to be definitely superior to any drug we have used heretofore, we feel that streptomycin is still a better all-around antituberculosis agent. Furthermore, experience with some 200 patients with various types and degrees of severity of tuberculous disease treated with isonicotinic acid hydrazids for periods ranging up to six months has failed to reveal a single case of disease arrested as the result of therapy with these drugs.

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AMEBIC ABSCESS OF THE FOOT

To the Editor:—Amebic infections of the skin have been described by some authors following the surgical treatment of amebic abscess of the liver (Heimburger, L. F.: *Arch. Dermat. & Syph.* **11**:49, 1925, and Van Hoof, L.: *Ann. Soc. belge de méd. trop.* **6**:45, 1926), the drainage after appendectomy (Cole, W. H., and Heideman, M. L.: *J. A. M. A.* **92**:537 [Feb. 16] 1929), or as anal amebiasis (Kouri, P.; Iriondo, M., and Peraza, J. A.: *Rev. Kuba* **5**:93, 1949). I have seen two patients with amebic infection of the foot, without any relation to intestinal amebiasis. The special conditions of the country must be mentioned: a very high percentage of the population are amebic "cyst-passers" and deposit the stools in the yards between the houses. The result is that in the dry season the dust contains the amebic cyst.

One patient, a 32-year-old Italian welder, was burned on the back of his right foot during working hours. After the wound was treated and a preventive penicillin injection was given he stayed at his home in the village for several days. When he came back to the infirmary, the wound was infected, there was necrotic tissue, and his foot was swollen. In the course of treatment the wound was cleaned out and penicillin and antitetanus vaccine were given. During the next week the patient was treated daily with penicillin, sulfadiazine tablets, and sulfathiazole powder, but the wound became deeper every day. Microscopic examination of the pus showed some streptococci and gram-negative bacilli. On the Giemsa-stained slides, ameba-like cells had been differentiated. The patient was called again, and a fresh drop of pus was examined. The Endameba histolytica cells were observed to have characteristic motility. Emetine hydrochloride, 0.04 gm. twice a day, was administered, without any other treatment. In three days a significant improvement was seen. After five days' application the treatment was terminated. On the seventh day the wound was closed with normal granulation tissue. Five days later the emetine treatment was repeated for three days (0.04 gm. twice a day). The patient was then observed for one year. The recovery was complete.

I saw the other patient after he was treated for several weeks by the village doctor. His physical condition was poor and he had fever and toxic symptoms. Blood cell count showed total

leukocytes 14,400, polymorphonuclear neutrophils 21%, basophils 6%, eosinophils 2%, monocytes 4%, lymphocytes 24%, and immature granulocytes 43% (myelocytes 26%, myeloblasts 17%). This picture, resembling myelogenous leukemia, was probably caused by the excessive doses of sulfonamides applied to control the infection of unknown origin. The Kahn reaction was negative. Blood smear (Giemsa stain) showed Plasmodium falciparum. On the sole of the patient's right foot was a deep fistulized abscess, which had started some weeks ago, when he stepped on a rusty nail. Microscopic examination of the pus revealed only E. histolytica. Antimalaria treatment was given. Antiamebic treatment was at that time not recommended because of the patient's general condition. The next day the fever decreased, and the second day it was normal. At the same time the amount of pus was decreasing. The wound was closed four days later without specific antiamebic treatment.

The probability of amebic wound infection is very high in this country. The low percentage of infection indicates that only special tissue conditions permit the amebic growth in the wound. In the cases cited here there was decreased tissue resistance caused by (*a*) local necrotic degeneration (high temperature burn) and (*b*) prolonged fever, with a high percentage of immature granulocytes in the bloodstream (malaria). Amebic skin infections are very responsive to the emetine treatment, but, as in the culture medium, amebas cannot grow in the wound without associated organisms. The long and incorrect way to treat amebic wound infection would be the elimination of the associated organisms. The correct method is to use emetine hydrochloride to control amebas and specific drugs for the associated organisms. In tropical countries examination of the fresh drop of pus is indicated in all cases of infected wounds resistant to the usual treatment.

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DIAGNOSIS OF LEPROSY

To the Editor:—In reference to a communication in The Journal of Aug. 23, 1952, page 1595, by Dr. H. W. Wade, statements are made concerning the diagnosis of leprosy. I had found that certain errors in diagnosis of leprosy are made not only because of faulty technique in obtaining material but also because of faulty staining of the smears.

The method that gives 100% accurate positive results is as follows: (Hansen's bacilli, being acid-fast, are stained by the Ziehl-Neelsen method, with attention to details, and with modifications.)

1. Within 10 to 20 minutes after smears are obtained fix over the flame of a Bunsen burner, passing three times.

2. Use an unscratched and properly cleaned defatted slide (with ethyl alcohol).

3. After fixation, flood slide with carbolfuchsin and steam (but do not boil) for 10 minutes (not 3 minutes as advised in textbooks). One must turn over the Bunsen burner and flame from above, not from below the slide (as stated in textbooks).

4. Shake off the stain (but do not wash at this moment in water as advised in textbooks). Immediately decolorize in hydrochloric acid (3%) in ethyl alcohol (70 to 80%) for three to five minutes and only then wash in tap water.

5. Stain with Loeffler's methylene blue for three minutes.

6. Wash the slide under tap water, shake off, and evaporate moisture by holding slide over high flame (but do not blot by filter paper as advised in the textbooks). A fine and clear picture is thus obtained.

As far as the technique of obtaining smears is concerned, Dr. G. W. McCoy, discoverer of Tularemia and professor of public health and preventive medicine at Louisiana State University, used a razor blade (in a manner similar to that described by Dr. Wade). The smears were given to me immediately. I stained and examined the material (personally and without any interference) with always 100% positive results, proving thus that dividing of responsibility must always be avoided for good results. Thus, in the case of suspected leprosy: the same physician must (1) obtain scrapings, after incision with a scalpel or razor blade (admixture of small amount of blood does not interfere with satisfactory results); (2) prepare all stains personally; (3) fix and stain all slides; and (4) examine microscopically. All errors could thus be avoided, provided close attention is paid by a properly trained worker.

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REACTION TO STREPTOKINASE AND STREPTODORNASE

To the Editor:—The unusual reaction to the intrapleural administration of streptokinase and streptodornase described by Baum and Oransky in The Journal, July 12, 1952, page 1012, has been observed although not reported previously (Miller and Long: *U. S. Armed Forces M. J.* 3:1061 [July] 1952). In essence, a large amount of fluid accumulates very rapidly in the pleural cavity. An outpouring of serum is one of the local reactions to streptokinase. This influx of fluid and the liquefaction of fibrin in the pleural cavity may displace the mediastinum and cause cardiorespiratory embarrassment if the accumulated fluid is not released.

The use of intercostal closed catheter drainage, in all but minimal instances of hemothorax, when streptokinase and streptodornase are injected, will prevent the reaction described by Baum and Oransky. The enzymes are dissolved in 20 cc. of sterile isotonic sodium chloride solution and injected through the catheter, which is then occluded for periods not exceeding eight hours to permit digestion. Suction of −6 to 8 cm. of water is applied to the catheter by a Stedman pump to remove the liquefied products and to encourage the lung to expand. Should untoward symptoms occur before the eight hours expire, the catheter can be opened to aspirate the fluid in the pleural cavity.

In a recent series of 12 patients suffering from hemothorax and treated with streptokinase and streptodornase, the temperature in all rose to between 101 F and 104.8 F. The cause of the fever is not known. Toxic effects accompanying the rise in temperature were not seen in these patients or in a large series of patients treated for various types of infection. That the untoward effects in the patient reported by Baum and Oransky were not due to the hyperpyrexia was shown by the prompt response of the patient to the aspiration of at first 2,300 cc. of serosanguineous fluid and later on the same day of 1,500 cc.

Baum and Oransky report on their patient as an instance of anaphylactoid shock. An allergic or an anaphylactoid response has not been seen in an extremely large series of patients treated with streptokinase and streptodornase. One of the principles of the surgical use of streptokinase and streptodornase is that of free drainage. This can be achieved in the pleural cavity by closed catheter drainage. Streptokinase and streptodornase offer the surgeon a valuable biological curette. They must, however, be properly used to achieve the desired result.

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PERIODICALS FOR FOREIGN PHYSICIANS

To the Editor:—Having been retired from active practice of my profession for a number of years I have derived considerable pleasure and interest from correspondence with men from foreign countries. The names and addresses of these men came to me through letters they had written to various sporting publications in this country asking for magazines of that type. In many cases they are not allowed to send money abroad for such purposes. I have a limited number of medical and surgical publications that I would gladly send abroad at my expense to either medical associations or contemporary practitioners.

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BUREAU OF LEGAL MEDICINE AND LEGISLATION

MEDICOLEGAL ABSTRACTS

Armed Services: Failure to Use Draftee as Physician.—The petitioner, a physician, sought, by a writ of habeas corpus, to compel his discharge from the United States Army, into which he had been drafted as a private. From a judgment of the district court denying the writ, the petitioner appealed to the United States court of appeals, ninth circuit.

Under the provisions of the Doctors Draft Law, the President of the United States was granted authority to ". . . require special registration of and, on the basis of requisitions submitted by the Department of Defense and approved by him, to make special calls for male persons qualified in needed—(A) medical and allied specialist categories who have not yet reached the age of fifty at the time of registration. . . . Persons called hereunder shall be liable for induction for not to exceed twenty-one [now 24] months of service in the Armed Forces." While under the terms of the general draft law, persons over the age of 26 are not eligible for induction, physicians, dentists, and allied specialists, in contrast with the general population, may be inducted up to the age of 50. The petitioner, a medical physician specializing in psychiatry, was over the age of 26 at the time of his induction. Prior to the date of his induction, on advice of the Selective Service System, and to avoid being inducted under the Doctors Draft Act, the petitioner applied for and was granted a commission as a captain in the Medical Corps, United States Air Force. This commission was revoked, however, two days before the date of his scheduled induction, because of the petitioner's failure to execute certain Air Force forms dealing with his commission application. Petitioner is presently a private in the Army of the United States, assigned to and a member of Enlisted Replacement Center, Fort Lawton, Wash., for shipment to the Far Eastern Command. Since his induction the Army has given petitioner a potential military occupational specialty of medical laboratory technician. Petitioner has repeatedly requested the Army to assign him work as a medical physician regardless of grade or rank but has been informed that Army regulations permit only commissioned officers to practice as physicians. Subsequent to his induction, the petitioner reapplied for a commission and that application is now pending. On being informed that it would take from six months to a year before his application was finally passed on, and the Army being unable, because of his noncommissioned status, to use him as a physician in the interim, the petitioner brought this petition to secure release from the Army.

The petitioner urges that a physician inducted under the act must be used as a physician in the armed services, that such requirement is mandatory under the act, and that, since his induction was for the one purpose only, if the Army cannot or will not give him such work, he must be discharged. His interpretation is based on the premise that the purpose of the act was to enable the armed services to secure needed medical, dental, and allied specialists, without unnecessarily depleting the short supply of such civilian persons, and that, consequently, to draft a physician and use him in another capacity is directly opposed to congressional intent because (1) the civilian supply is depleted and (2) the military demand remains unsatisfied. To give the statute any other construction, the petitioner argued, would render it unconstitutional. That the primary purpose of drafting physicians, not otherwise subject to induction, was to supply the armed forces with needed specialists in this category, said the court of appeals, is apparent. Certainly, that was the ground on which the bill was justified to Congress by the military. And it also seems apparent that Congress contemplated that inductees under the act would normally be utilized in their professional capacities.

The case was argued and briefed by the government on the broad theory that, under the statute, physicians could be drafted and used for any purpose the Army saw fit; that the matter of duty assignment for such inductees was simply a matter of military discretion. In response, the petitioner urged that such a construction renders the act subject to constitutional attack as unreasonable and discriminatory class legislation. We find it unnecessary to decide the constitutional question, said the court of appeals. The petitioner is not being utilized in a capacity wholly outside the medical field. While it is true that under Army regulations he cannot practice medicine as such, he is nevertheless being employed in a type of work for which his medical training renders him particularly adaptable. There are many specialized duty assignments within the armed forces that require the performance of tasks well within the competence of physicians due to their extensive medical training. Such assignments may well be criticized as wasteful because they are not utilizing the inductees capacities to the full level of his ability, but they are nevertheless within the area of his special competence. We think, the court concluded, that a construction that the military may make such duty assignments is as far as we need go in this case.

The words of the statute, in terms, do not require plaintiff's construction that a particular type of work alone can be assigned to inductees. Nor do they, in terms, require that a commission be granted inductees. On the contrary, it may well be urged that the words used will not bear the meaning that the petitioner seeks to impress on them. The act seems merely, by acting within the framework of the general law, to describe additional classes of men eligible for induction under the latter statute. There is nothing to indicate that men inducted under this new section of the draft law are to be treated, after entrance into the armed forces, differently from men inducted under other provisions. We do not think that the words of the statute preclude the Army's present utilization of the petitioner.

The legislative history of the act bears out this construction. Congress was deeply concerned over the use that would be made by the armed forces of inductees and that the military should not waste their talents. Justification for the bill as written and the allaying of congressional fears was accomplished by assurances from the military that men inducted under the act would be used in their professional capacities. These assurances were, in turn, used as arguments for passage of the bill during the debates. The necessity for such reassurances implies a congressional recognition that, as written, the bill simply described a new class of persons eligible for induction and did not make mandatory use of the inductees strictly in their professional capacities. We think Congress passed the bill in the form it did relying on the good faith of the military's representations that professional talents of the inductees would be effectively utilized. Petitioner having been given a duty assignment within what we find to be the minimal permissible area, we are without power to control the exercise of military discretion.

Problems of a similar nature to that presented in this case were discussed before Congress. Representatives of the American Medical Association and American Dental Association were concerned that men might be inducted under the act before their applications for commissions were acted on. A bill was introduced in the House, and died in committee, that would have prohibited induction of a registrant until he had been tendered a commission. It was recognized that a man could not be inducted into a commissioned status but would have to be drafted as a private. General Robinson, Surgeon General of the Army, testified before the House committee that on being drafted it would be Army policy to tender a commission to the inductee but that it could be done only if he would accept it. Representative Kilday asked: "If he would not accept it he would remain on as an enlisted man?" General Robinson replied: "That is correct." Congress then was not unaware of the problems that might arise in the case of men inducted, necessarily as privates, under the act. Yet, as eventually adopted, the bill bears silent witness to the rejection of legislative proposals specifically designed to deal with such situations. It seems apparent, however, that the induction of a physician without the tendering of a commission is and will continue to be a very exceptional case indeed. The Medical Corps of the Air Force in this case went out of its way to have the petitioner commissioned before induction, by postponing certain requirements in order to accomplish this. It was petitioner's refusal to comply with regulations that resulted in his commission being revoked. Petitioner cannot be said to be without fault in causing the situation in which he now finds himself. Nor is the Army to be censured in this particular case. It found itself with an inductee sent by the Selective

Service Board, which it could not, because of regulations, use as a physician in a full sense. We have not been advised as to how the Army could legally discharge the inductee under such circumstances. It has him on its hands and is using him in a capacity employing some of his skills. We see no more it could do.

Accordingly the judgment denying the petitioner's request for discharge was approved. *Orloff v. Willoughby, 195 F. (2d) 209 (1952).*

Tuberculosis: Compulsory Examination vs. Religious Freedom. —This was a mandamus proceeding to compel the Board of Regents of the University of Washington to permit registration of a student at the university without submitting to an x-ray examination of the chest. From a judgment denying the writ, the plaintiff appealed to the Supreme Court of Washington.

Since 1941, the Board of Regents of the University of Washington has required all entering freshmen to undergo an x-ray examination of the chest for the purpose of discovering possible tubercular infection and as a condition precedent to registration. The plaintiff entered the university in 1947 as a freshman and, after voicing her objections, submitted to the examination. In 1950, on the advice of the health officer of the university, the board of regents extended its requirement to all students desiring to register. When the plaintiff applied for registration for her senior year, she refused to comply with this new rule. The plaintiff is a member of the Christian Science church and adheres to its doctrine, and she requested exemption from the examination because of her belief that submission to it is contrary to that doctrine and to her personal religious convictions. At the hearing in the trial court, the health officer of the university testified to certain facts regarding the nature of tuberculosis, its incidence on the university campus, and the reasons for making the requirement in question. His testimony was uncontroverted and, in summary, was that tuberculosis is an insidious, slow, and progressive disease and is infectious; that a person may be infected with it and show no symptoms of the disease nor be aware of his infection; that its early discovery is difficult, except by x-ray examination of the chest; that this method of exploration is generally considered best adapted to mass screening by the medical profession; that a tubercular lesion in the lungs will show as a shadow upon an x-ray film; and that further tests will then permit a positive diagnosis. He stated it to be his conclusion that, in order to protect the health of the student body, it is imperative that every effort be made to discover the presence of the disease on the campus and that for this purpose the requirement of an x-ray examination of all registering students is necessary. The plaintiff raised two questions: the constitutionality of the regulation and the power of the board of regents to make the regulation.

The material portion of the first amendment to the constitution of the United States is: "Congress shall make no law respecting an establishment of religion, or prohibiting the free exercise thereof; . . ." Amendment 4 to the constitution of the state of Washington provides, in part: "Absolute freedom of conscience in all matters of religious sentiment, belief and worship, shall be guaranteed to every individual, and no one shall be molested or be disturbed in person or property on account of religion; but the liberty of conscience hereby secured shall not be so construed as to excuse acts of licentiousness or justify practices inconsistent with the peace and safety of the state." Religious freedom, said the Supreme Court, embraces two concepts, freedom to believe and freedom to act. The first is absolute, but, in the nature of things, the second cannot be. Conduct remains subject to regulation for society's protection. This freedom can be restricted only to prevent grave and immediate danger to interests the state may lawfully protect.

With these principles in mind, continued the Supreme Court, we cannot say that the questioned regulation violates any constitutional inhibition. Here the public interest threatened is the health of all of the students and employees of the university. It may lawfully be protected. In this case, it is of more importance than the right of the plaintiff that is infringed. The danger to this interest is clear and present, grave and immediate. Infringement of plaintiff's rights is a necessary consequence of a practical attempt to avoid the danger. The questioned requirement utilizes the generally approved method of combating the danger, and no practical method that might not possibly infringe a constitutional right is shown. It is a regulation pertaining to the second aspect of the constitutional inhibition, in which aspect the conduct of the plaintiff is subject to regulation for the protection of others. Her "freedom to believe" remains absolute.

The second contention raised by the plaintiff related to the power of the board of regents to make this regulation. By authority of the statutes of the state, the board of regents has vested in it the government of the university. These statutes provide in part: ". . . First. The said board shall have full control of the university. . . ." The protection and improvement of the health and physical condition of the students is as much the responsibility of the regents as is their mental training and development. They cannot neglect the former and expect the latter to flourish. It is their duty to provide for both. Because power to make and enforce reasonable health regulations affecting all students is indispensable to the continued operation of the institution, it must have been the legislative intent that such power be implied in the general grant of "full control of the university." The close contact among the students and between the students and the faculty in the classroom and in other places of assembly on the campus, the wide diversity of places from which the students come, and their various conditions of physical health and development must have been in the mind of the legislature when the government of the university was lodged in the board of regents. At least, it must have been intended that they would not permit an infectious disease to spread on the campus, if a way to prevent its doing so became known to them. We therefore conclude, said the Supreme Court, that the board of regents had the power to make and enforce the regulation in question, and that the disallowance of the exemption claimed by the plaintiff was proper.

(In a dissenting opinion, two justices disagreed with the majority as to the existence of a "clear and present danger" so far as tuberculosis is concerned. What is a clear and present danger, asked the dissenting judges. First, they said, it must be a danger of some "extremely serious" substantive evil. Second, the danger must be "clear," that is, there must be proof that the evil will almost inevitably result from the particular exercise of freedom. Third, the danger must be "present," that is, the "degree of imminence extremely high." These expressions concerning the clear-and-present-danger rule, said the dissenting judges, set an extremely strict test. It must be readily granted that the thing sought to be guarded against, infection with tuberculosis, is an extremely serious substantive evil. But is there a clear and present danger, as defined above, that this evil will result if the plaintiff and those who are like situated are exempted from the x-ray examination in question? Will other students at the university "almost inevitably" contract tuberculosis if the plaintiff and others sharing her religious beliefs are not screened before the x-ray machine once a year? Will such danger "immediately" [as distinguished from remotely or even probably] imperil other students? It was the opinion of the dissenting justices that there was no fact or consideration stated in the majority opinion that would justify an affirmative answer to these questions. It was the health officer's view that a single case of tuberculosis is an "epidemic," if it can be prevented. This interesting conception of the term "epidemic," said one of the dissenting judges, doubtless evidences an admirable frame of mind in one charged with supervising the health of university students. But this court cannot consider itself bound by such an extreme view when confronted with the task of adjusting a conflict between the exercise of police power and the enjoyment of guaranteed liberties. Those of us who attended the university prior to 1941, when the x-ray program was first set up, did not then consider that we were facing a clear and present danger of contracting tuberculosis. We were certainly not so advised by health authorities. How can it be, then, that in 1950 and 1951, with the incidence of tuberculosis dwindling and most of the campus population regularly taking the x-ray examinations, there has come into being a clear and present danger that the students will be infected by the tiny fraction who seek exemption on religious grounds?)

In accordance with the majority opinion, however, the judgment of the trial court in favor of the board of regents of the university and sustaining its right to require x-ray examination of all registering students was affirmed. *State v. Armstrong, 239 P. (2d) 545 (Washington 1952).*

MEDICAL LITERATURE ABSTRACTS

UNITED STATES

A.M.A. Arch. Dermat. and Syphilol., Chicago

66:1-144 (July) 1952

Neurogenic Factors in Contact Dermatitis. W. B. Guy.—p. 1.
*Tinea Capitis in the Adult and Adolescent. J. L. Pipkin.—p. 9.
Erythema Multiforme Following Deep X-Ray Therapy. J. Davis and G. T. Pack.—p. 41.
Pemphigus Vulgaris: Clinical and Laboratory Study. I. Fisher.—p. 49.
Aureomycin and Its Effect in Early Syphilis: One-Year Progress Report. J. Rodriquez, S. Weinstein and G. E. Parkhurst.—p. 59.
Mouse Ringworm. B. H. Booth.—p. 65.
Clinical Experience with "Polycin," Polymyxin-Bacitracin Ointment. F. M. Gastineau and H. J. Florestano.—p. 70.
Association of Carcinoma and Mycosis Fungoides. S. M. Bluefarb, R. Ihrke and H. S. Steinberg.—p. 76.
*Significance of Acanthosis Nigricans. H. O. Curth.—p. 80.
Exfoliative Dermatitis Due to Banthine®. R. F. Clark and D. W. McNaughton.—p. 101.
Multiple Pesticides for Scabies and Pediculosis. T. Cornbleet, H. C. Schorr and B. Firestein.—p. 103.
Experimental Evidence and Clinical Studies as Basis for Nomenclature in Frambesia Tropica (Yaws). C. M. Hasselmann.—p. 107.

Tinea Capitis in Adult and Adolescent.—The incidence of tinea capitis caused by Trichophyton tonsurans (crateriforme species) infections is especially high in Texas and Southern California, probably as a result of spreading from Mexico and Central America. Other endemic foci are found in Oklahoma, Utah, Georgia, and the southern half of the United States. Microscopic demonstration of spores around or in the hair confirmed the clinical diagnosis in 64 postpuberal patients (4.9% of the author's series of 1,304 cases observed during the 20 years from 1931 to 1951). Infection was due to Microsporum and Trichophyton organisms, with the T. tonsurans (crateriforme) group predominating. Organisms of this group may produce a variety of bizarre clinical manifestations, especially in adults, which frequently suggest other diseases. Classic forms in this series were exceptional. Concomitant glabrous skin lesions and nail involvement were commonly found in both adults and adolescents. The only clue to the diagnosis of ringworm that was always present in this series was an infected stub or hair. Microsporum infections responded to local treatment. Topical treatment in most cases of infection due to T. tonsurans, however, was useless unless a certain amount of inflammatory reaction was present when the patient first came under observation. Roentgen epilation (390 to 410 r to 5 points) followed by thorough manual removal of the stubs, dots, and fragments of hair is the treatment of choice in noninflammatory Trichophyton infections.

Significance of Acanthosis Nigricans.—Two types of acanthosis nigricans occur: the malignant type, which is always associated with internal adenocarcinoma, and the benign type, which has no such association. Benign acanthosis nigricans begins at birth or in childhood or appears at puberty. It is always accentuated during the adolescent period, either regressing or remaining stationary when adolescence is over. Malignant acanthosis nigricans may occur in children, but most patients are adults when the first signs appear. The skin lesions may either precede or follow the internal cancer, or coincide with its manifestations. Treatment of the cancer may result in a temporary improvement in the skin lesions but on recurrence of the tumor or the development of metastases they reappear. The skin lesions of about 20% of the patients with malignant acanthosis nigricans appear before any signs of cancer can be noted, several years sometimes elapsing before the internal cancer becomes manifest. These patients thus provide an excellent opportunity for the experimental study of early cancer changes in the body. The cancers associated with acanthosis nigricans, which are all adenocarcinomas although they may originate in various organs, are highly malignant, with a mortality rate of 100% and an average duration from discovery to death of less than one year. A pseudo acanthosis nigricans may occur in the body creases of obese brunette persons. This condition apparently depends on factors accompanying obesity, because it develops when the patient gains weight and disappears when he loses it. Pseudo acanthosis nigricans should be differentiated from true acanthosis nigricans so that patients may be spared the needless anxiety of believing they have a cancer-related disease, and so that a rational system of treatment may be instituted.

A.M.A. Arch. Internal Medicine, Chicago

90:1-136 (July) 1952

Cerebral Metabolic Disturbance and Delirium in Pernicious Anemia: Clinical and Electroencephalographic Studies. D. C. Samson, S. N. Swisher, R. M. Christian and G. L. Engel.—p. 4.
*The Dying Human Heart: Electrocardiographic Study of 43 Cases, with Notes upon Resuscitative Attempts. C. D. Enselberg.—p. 15.
Spontaneous Chylothorax: Observations on Its Pathogenesis and Management Based on Study of Five Cases. R. H. Meade.—p. 30.
Endemic Infectious Hepatitis in an Infants' Orphanage: II. Epidemiologic Studies in Infants and Small Children. A. M. Bennett, R. B. Capps, M. E. Drake and others.—p. 37.
Essential Thrombophilia. R. W. Monto, W. D. Griest and D. E. Szilagyi.—p. 54.
*Results of Cortisone-Corticotropin Therapy in Chronic Active Rheumatic Fever. D. Young and M. Rodstein.—p. 64.
Allergy—Corticotropin and Cortisone: Review of Literature from September, 1950, to January, 1952. R. R. Evans and F. M. Rackemann.—p. 96.

Electrocardiographic Study of the Dying Human Heart.—Electrocardiograms were recorded for various lengths of time before, during, and after death in 43 patients. In 25 heart disease was the primary cause of death, and 17 of these 25 had myocardial infarction. The terminal electrocardiogram generally follows a pattern unrelated to the underlying disease. Lower pacemakers predominate until irregular idioventricular rhythm with gradual slowing appears. Termination in ventricular fibrillation occurs in one-fifth to one-third of the patients. Recurring asystoles or ventricular standstills are common and often appear to be self-limited. The following unusual findings were described: (1) auricular flutter and fibrillation succeeding sinus rhythm (four cases); (2) bidirectional ventricular tachycardia with alternation of RS-T segment and T waves only (one case); (3) paradoxical shortening of the Q-T interval (three cases); and (4) progressive shifts of RS-T junction and segment (three cases). Resuscitative measures were used in 22 cases, but their evaluation was difficult in view of the frequency of recurring self-limited asystoles. The intracardiac use of epinephrine should be avoided until other measures have been exhausted. These include intravenous and intra-arterial blood transfusion and artificial respiration with oxygen. Resuscitation from ventricular fibrillation requires immediate surgical exposure for the purpose of manual cardiac massage and electric defibrillation, together with procedures to support blood pressure and respiration.

Cortisone-Corticotropin Therapy in Chronic Active Rheumatic Fever.—Eight children with chronic active rheumatic fever were treated with cortisone or corticotropin (ACTH) for prolonged periods. One patient died while still receiving cortisone, and autopsy revealed an active, healing rheumatic process in the lungs. In five patients the process continued to be active after cessation of therapy, and in none of these patients was the dura-

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Titles marked with an asterisk (*) are abstracted.

tion of the disease apparently shortened, although the severity of the disease was diminished in four. One patient, desperately ill, had his rheumatic process terminated by therapy and has remained well for more than a year. A severe rheumatic process was terminated also in one other patient, with no reactivation over a year's time. Congestive heart failure refractory to all other therapeutic attempts was cleared entirely in four of five patients. The degree of cardiac involvement was never diminished by therapy. Four patients had evidence of additional organic heart disease during or shortly after treatment. The usual nonspecific effects of adrenocortical therapy on fever and general well-being were observed in the majority of patients. The common side-effects of these drugs were also observed and are considered of no clinical significance except for gastrointestinal hemorrhage and hypokalemia. The authors conclude that to anticipate complete quiescence of chronic active rheumatic fever by treatment with cortisone or corticotropin is speculative. At times total quiescence may be achieved, but a disappearance of the manifestations of congestive heart failure, despite a persistence of some activity of the disease, is more common. In some children with severe disease prolonged administration of large doses may be lifesaving.

A.M.A. Arch. Ophthalmology, Chicago

47:695-836 (June) 1952

Narrow-Angle Glaucoma. P. A. Chandler.—p. 695.
Cytochrome-C Content of Bovine Crystalline Lens. L. O. Ely.—p. 717.
Evaluation of Capillary Mechanisms in Primary Glaucoma. A. H. Keeney and I. H. Leopold.—p. 720.
Cytology of Allergic Conjunctivitis. S. A. Hanser, W. A. Moor and A. W. Stickle.—p. 728.
Possible Malignant Melanoma of Choroid. J. A. deVeer.—p. 734.
Relationship Between Accommodation and Convergence. M. W. Morgan Jr.—p 745.
Fibrous Components of Vitreous Body. A. Grignolo.—p. 760.
Fixation Anomalies in Amblyopia. F. W. Brock and I. Givner.—p. 775.
Evaluation of Local Cortisone Therapy in Ophthalmology. M. Fine and R. C. Goodwin.—p. 787.

48:1-126 (July) 1952

Ocular Periarteritis Nodosa: Report of Two Cases. G. N. Wise.—p. 1.
Studies on Crystalline Lens: V. Distribution of Various Phosphate-Containing Compounds and Its Significance with Respect to Energetics. C. E. Frohman and V. E. Kinsey.—p. 12.
Aberrant Intraocular Adenomata and Epithelization of Anterior Chamber. L. Christensen and E. D. Anderson.—p. 19.
Retinal Detachments Occurring in Cataract Associated with Neurodermatitis. R. S. Coles and J. Laval.—p. 30.
Iridoschisis: Report of Additional Case. G. M. Haik, W. Lyda and R. L. Waugh.—p. 40.
*Retrolental Fibroplasia: Negative Role of Light, Mydriatics, and the Ophthalmoscopic Examination in Its Etiology. J. C. Locke and A. B. Reese.—p. 44.
Use of Erysiphake for Deeply Embedded Corneal Foreign Bodies. L. T. Jones and J. Goldman.—p. 48.
Disparity Limits of Stereopsis. K. N. Ogle.—p. 50.
Primary Calculus of Lacrimal Sac: Report of Case. S. Weizenblatt.—p. 61.
Benign Pigment-Epithelium Tumor of Iris. J. Laval.—p. 66.
Rotator and Illuminator for Pseudoisochromatic Plates. I. Schmidt and H. Fleck.—p. 75.
*Prevention of Retrolental Fibroplasia. V. M. Crosse and P. J. Evans.—p. 83.

Retrolental Fibroplasia.—One eye of each of 22 babies whose weight at birth was 2,000 gm. or less was covered with a firm gauze and adhesive patch in a manner that would shut out all light. This was done within 24 hours after birth. The patch was not removed until the time of discharge from the hospital, an average of 46 days after birth. During this time the unbandaged eye was examined with the ophthalmoscope once a week if normal and three times a week if signs of early retrolental fibroplasia appeared. Ten babies showed manifestations of the acute phase of retrolental fibroplasia in the unpatched eye during the period of monocular occlusion. Subsequent examination of the occluded eyes revealed almost identical changes, with only minor variations in severity. The monocular-occlusion experiments, therefore, revealed no evidence suggesting that absence of exposure of one eye to light prevented retrolental fibroplasia in that eye, or lessened the severity of the disease in that eye with respect to the other. Firm adhesive and gauze patches were applied binocularly within 4 to 24 hours after birth to the eyes of 33 premature infants with a birth weight of 1,800 gm. or less. At the time of discharge from the hospital, the patches were removed and the eyes examined ophthalmoscopically. Manifestations of the acute phase of retrolental fibroplasia were observed in 15 at the time of the first ophthalmoscopic examination. There was no significant decrease in the incidence of the disease in the group whose eyes were patched and were not examined or treated with mydriatics, as compared with the incidence in a group of babies from the same nursery born during an immediately preceding period who had received weekly ophthalmoscopic examinations, through widely dilated pupils, from birth. The results of these experiments would seem to demonstrate that instillation of mydriatrics, premature exposure of the eyes to light, and handling of premature babies for routine ophthalmoscopic examination are not factors in production of retrolental fibroplasia.

Prevention of Retrolental Fibroplasia.—In Great Britain the number of cases of retrolental fibroplasia has risen rapidly since the disease was first reported there, in 1946. The incidence differed in onset and progression in different centers, but as in the United States, its occurrence was restricted almost entirely to centers with special units for premature babies. Furthermore, the occurrence of cases coincided either with the increased use of oxygen in established units or with the setting up of new units with full facilities for oxygen administration. The only change in treatment of premature infants in the years 1946 to 1951 that showed any significant relation to retrolental fibroplasia was the amount and duration of oxygen administration. The survival rate changed little between the period from 1946 to 1948, when there was little use of oxygen and the period of January, 1949, to June, 1950, when oxygen was used freely, but has improved quite considerably in the period of July, 1950, to December, 1951, during which oxygen administration was reduced. The increase of retrolental fibroplasia followed closely the period of free use of oxygen and subsided again with its restriction. For the last 15 months treatment by one of the authors of premature infants involved administration of minimal doses of oxygen for the shortest possible time while a graduated return to normal air was achieved as soon as possible. Just enough oxygen was given to prevent cyanosis. Of 11 babies so treated, 6 survived and there was not a single case of retrolental fibroplasia, while of 27 infants treated with much oxygen during the previous period 13 survived and 3 had retrolental fibroplasia. The authors consider it right to draw attention to the dangers of the use of too much oxygen and to its administration for too long a period. They conclude that while other factors, at present unknown, may contribute to the establishment of retrolental fibroplasia, a revision of the policy of oxygen administration to premature infants of low birth weight can very largely exclude, by prevention, the disease.

American J. Digestive Diseases, Fort Wayne, Ind.

19:161-200 (June) 1952

Relationship Between Histological Lesions and Radiological Signs of Cancers of Mucous Membrane of Stomach (Cancers Localized in Mucous Membrane and Not Having Spread to the Wall: Stage I). G. Albot and J. Toulet.—p. 161.
Why Not Better Types of Stool Examinations? A. Bassler.—p. 169.
Tumoral Hypertrophy of Gastric Mucosa: Case Report and Summary of Findings. P. T. Dolan and P. H. Sherman.—p. 171.
*Post-Necrotic (Toxic) Cirrhosis: Its Clinical Significance. L. A. Stine and J. M. Swarts.—p. 176.
New Anti-Ulcer Drug: Clinical and Radiological Evaluation. M. P. Rogers and C. L. Gray.—p. 180.
Hypercholesterolemia and Senescence. E. M. Abrahamson.—p. 186.
Fecal Impaction: Report of Case Due to Wild Grape Seeds and Elderberry Stems. R. H. Burnikel and H. C. Sprecher.—p. 191.

Postnecrotic Cirrhosis.—A study of 6,184 necropsy records for the period 1931-1949 disclosed 10 cases (0.17%) that conformed morphologically to the postnecrotic (toxic) type of cirrhosis, among 95 cases of cirrhosis of all types. The clinical records of the 10 cases were compared with those of 386 cases of Laennec's cirrhosis reported on by Ratnoff and Patek in 1942. There was, however, little apparent difference in the antecedents and courses of the two conditions, and it is unlikely that an accurate clinical differentiation can be made between them. The only difference in the principal clinical signs of the two conditions was the commoner occurrence of ascites with its associated gastrointestinal symptoms of weight loss, anorexia, nausea, and

vomiting in the group with Laennec's cirrhosis. Ascites was detectable in 301 cases (78%) of this group, but in only 3 of the authors' 10 cases. It is questionable, however, whether this statistical difference would be helpful in the differential diagnosis in an individual case.

American Journal of Medical Sciences, Philadelphia

224:1-120 (July) 1952

Observations on Etiologic Relationship of Achylia Gastrica to Pernicious Anemia: XIV. Intrinsic Factor Activity of Desiccated and Defatted Human Fundus, Duodenum, and Jejunum. E. Landboe-Christensen, L. Berk and W. B. Castle.—p. 1.
Treatment of Sprue with Folinic Acid: Report of Nine Cases. C. A. Romero, R. Vizcarrondo and R. Rodriguez-Molina.—p. 9.
Sedimentation Rate in Myocardial Infarction. M. Plotz.—p. 23.
Effect of Quantitative Variations of Anticoagulant Solutions upon Prothrombin Time. B. W. Volk and S. Losner.—p. 27.
Small Vessel Dysfunction in Patients with Diabetes Mellitus: I. Skin Temperature Response to Priscoline in Toes of Diabetics. M. B. Handelsman, L. M. Levitt and H. Conrad Jr.—p. 34.
Id.: II. Retinal Vessel Response in Diabetics Following Priscoline. M. R. Choist, L. M. Levitt and M. B. Handelsman.—p. 39.
Effects of Hydrogenated Alkaloids of Ergot on Vasomotor Reflexes. T. Winsor.—p. 42.
*Effect of Para-Aminosalicylic Acid (PAS) on Development of Resistance of Tubercle Bacilli to Streptomycin. B. Friedman, L. Sale Jr. and A. Goldman.—p. 53.
Anthrax Meningitis: Review of Literature and Report of Two Cases with Autopsies. T. H. Haight.—p. 57.
Clinical Trial of Prodigiosin in Disseminated Coccidioidomycosis. R. H. Wier, R. O. Egeberg, A. R. Lack and G. M. Leiby.—p. 70.
*Pasteurella Multocida in Suppurative Diseases of Respiratory Tract. A. M. Olsen and G. M. Needham.—p. 77.
Hereditary Spherocytosis (Congenital Hemolytic Jaundice): Pathogenesis of "Hemolytic" Crisis. J. D. Battle Jr.—p. 82.
Coxsackie Viruses and Human Disease. E. D. Kilbourne.—p. 93.
Psychiatric Aspects of Sexual Disturbances. A. J. Silverman.—p. 103.

p-Aminosalicylic Acid and Resistance of Tubercle Bacilli to Streptomycin.—The development of bacterial resistance is an obstacle to the use of streptomycin and dihydrostreptomycin in the treatment of tuberculosis. This report is concerned with the development of bacterial resistance under three treatment regimens: 24 patients received dihydrostreptomycin; 25 dihydrostreptomycin and *p*-aminosalicylic acid; and 25 streptomycin and *p*-aminosalicylic acid. Streptomycin or dihydrostreptomycin was given in doses of 1 gm. daily intramuscularly for 13 weeks. *p*-Aminosalicylic acid was given by mouth in four equal doses totaling 10 gm. a day. The drug was neutralized by the addition of sodium bicarbonate, 6 parts to 10 parts of *p*-aminosalicylic acid. In order to readily obtain positive cultures, patients with far advanced pulmonary tuberculosis were selected for study. Cultures were made from sputum or gastric contents. It was found that the addition of *p*-aminosalicylic acid to streptomycin or dihydrostreptomycin greatly delays the emergence of resistant organisms. Combined therapy for a period of three months results in decrease in resistant organisms during this interval and for three months thereafter. The addition of *p*-aminosalicylic acid to streptomycin or dihydrostreptomycin increases the number of sputum conversions both during the treatment period and the subsequent three months.

Pasteurella Multocida in Suppurative Diseases of the Respiratory Tract.—Some species of the genus Pasteurella, which includes the causative agents of tularemia and bubonic plague, are responsible for epidemics of hemorrhagic septicemia in animals. "Shipping fever" and "fowl cholera" are terms often applied to these infections. The genus and species name, Pasteurella multocida, has been assigned to organisms capable of producing hemorrhagic septicemia. Hemophilus influenzae may closely resemble Past. multocida and the gross appearance of the colonies of Past. multocida simulates that of colonies of certain strains of Klebsiella. These resemblances may account for some erroneous diagnoses. Past. multocida was isolated in 37 cases observed at the Mayo Clinic in nearly five years. Twenty-seven of the 37 patients were either farmers or members of a farmer's family. Nearly all came from rural communities. Bronchiectasis was the clinical diagnosis in 30 of the 37 patients, and bronchial secretions, sputum, or empyema fluid were in most cases the source material from which Past. multocida was isolated, although the organism was detected also in one case each of abscess of the frontal sinus, appendiceal abscess, and the drainage from a gouty joint. Past. multocida, which proved sensitive to low concentrations of penicillin, was probably not the causative agent of the pulmonary infections encountered but merely a "secondary invader." Nevertheless, the finding of animal strains of Pasteurella in humans is significant. The organism is usually the predominant pathogen when it occurs in the cultures of bronchial secretions or empyema fluid. It usually occurs in persons who have ample opportunity for contact with infected animals. Furthermore, Past. multocida is rapidly eradicated by penicillin therapy, and clinical improvement usually has been observed after the administration of this antibiotic.

American Journal of Medicine, New York

13:1-120 (July) 1952

Thrombotic Thrombocytopenic Purpura. B. R. Gendel, J. M. Young and A. P. Kraus.—p. 3.
*Hemostatic Defect in Thrombocytopenia as Studied by Use of ACTH and Cortisone. W. W. Faloon, R. W. Greene and E. L. Lozner.—p. 12.
*Effect of Corticotropin (ACTH) and Cortisone on Idiopathic Thrombocytopenic Purpura. S. J. Wilson and G. Eisemann.—p. 21.
Hypercoagulability of Blood of Patients with Hepatic Cirrhosis Following Administration of ACTH. W. J. Eisenmenger, R. J. Slater and A. M. Bongiovanni.—p. 27.
Chronic Hypoplastic Neutropenia. T. H. Spaet and W. Dameshek.—p. 35.
Mediterranean Hemopathic Syndromes (Cooley's Anemia) in Adults: Study of a Family with Unusual Complications. H. W. March, S. M. Schlyen and S. E. Schwartz.—p. 46.

Hemostatic Defect in Thrombocytopenia.—Four patients with idiopathic thrombocytopenic purpura and three with purpura and thrombocytopenia associated with leukemia were studied during treatment with corticotropin (ACTH) or cortisone. Results indicated that these drugs induce improvement in vascular resistance, which is not necessarily accompanied with increased platelet production. Although complete remission with normal platelet counts, prothrombin utilization and clot retraction occurred in two patients, this was preceded by improvement in vascular resistance in both. In all other patients vascular resistance increased without the occurrence of a corresponding improvement in the platelet count. Administration of corticotropin or cortisone did not interfere with either a spontaneous remission in one patient or remission induced by splenectomy in three patients. The hematological changes occurring during remission induced by corticotropin did not appear to differ from those observed during a spontaneous remission in a patient not receiving corticotropin or cortisone. The hemostatic defect in thrombocytopenia thus appears to be due to (1) abnormal vascular fragility, which has been consistently responsive to adrenocortical steroid mobilization or administration, and (2) to reduced production or increased destruction of platelets, with concomitant poor clot retraction and prothrombin utilization, which are only irregularly corrected by hormone therapy. The results obtained in the authors' patients suggest that corticotropin or cortisone may be beneficial in acute episodes of thrombocytopenia, in preparing patients for splenectomy, in producing improvement of persistent or recurrent thrombocytopenia and purpura after splenectomy, and in symptomatic relief of patients with leukemia associated with thrombocytopenia and hemorrhagic diatheses.

Corticotropin and Cortisone in Idiopathic Thrombocytopenic Purpura.—Twelve patients with idiopathic thrombocytopenic purpura were given corticotropin (ACTH) in doses of 40 mg. per day intramuscularly or cortisone in doses of 50 to 100 mg. daily. Five had a complete clinical and hematological remission. Of these five patients, one had previously had a splenectomy with recurrence of the disease; he responded completely to corticotropin, while cortisone had little effect on the platelet level. Another patient who responded to corticotropin and later to splenectomy had subsequent recurrence of thrombocytopenic purpura. Another patient responded to both corticotropin and cortisone. Two others responded to cortisone. There was no recurrence of thrombocytopenic purpura in these three patients. Seven patients did not respond to the hormones. Splenectomy was done in six of these patients, with excellent clinical and hematological responses in five. Various hypotheses of the actual role of corticotropin and cortisone in the control of certain cases of idiopathic thrombocytopenic purpura have been advanced, but at present the mode of action of the hormones in these cases is unknown.

American Journal of Ophthalmology, Chicago

35:755-916 (June) 1952

Neuromyelitis Optica. G. I. Scott.—p. 755.
Etiologic Study of Series of Optic Neuropathies. C. H. Bagley.—p. 764.
Lacrimal Fluid in Keratoconjunctivitis Sicca: Quantitative and Qualitative Investigation. J. Balik.—p. 773.
Low Flow of Tears—Dry Eye. A. F. M. de Roetth.—p. 782.
Physiopathology and Technique of Iridencleisis. S. J. Meyer.—p. 788.
Significance of Alternating Hypertropia in Concomitant Strabismus. A. Schlossman.—p. 795.
Study of Mode of Action of Filatov's Method of Tissue Implantation. J. G. Van Manen.—p. 801.
Verhoeff's Theory of Anomalous Projection. Z. W. Colson.—p. 807.
Osteogenic Sarcoma Following Irradiation for Retinoblastoma: With Report of Case. R. D. Tebbet and R. D. Vickery.—p. 811.
Comparison of Vision Screening Tests with Clinical Examination Results. A. E. Sloane and J. R. Gallagher.—p. 819.
*Retinal Findings in Pregnancy Complicated by Diabetes Mellitus and Toxemia. S. S. Snyder.—p. 831.
Ocular Findings in Lupus Erythematosus. J. S. Aiello.—p. 837.
Epithelial Plaques of Conjunctiva. R. J. Kennedy and J. V. Sullivan. —p. 843.
Comparison of Effect of Low (124 K. V.) and of High (30 MEV.) X Irradiation on Incidence of Lens Opacities in Mice. L. B. Clark and P. Sykowski.—p. 848.

Retinal Findings in Pregnancy Complicated by Diabetes and Toxemia.—From 1939 to 1950 a total of 131 pregnancies observed at the New York Lying-In Hospital were complicated by diabetes. Thirty-seven women had a concomitant toxemia and the eyegrounds of these patients had been examined and the results recorded. An analysis of these cases convinced the author that daily ophthalmoscopic examinations are another aid to the obstetrician in the management of patients with diabetes mellitus and a toxemia of pregnancy. It is relatively safe to allow pregnant patients with diabetes and mild preëclampsia to deliver spontaneously or near term unless more pronounced retinal arteriolar changes develop. If the patient has severe preëclampsia with grade 1 retinal arteriolar changes and the baby is large enough, labor should be induced or cesarean section done before grade 2 changes appear. Pregnant diabetic women with mild hypertension can safely deliver at term unless toxemia develops with arteriolar alterations. Severe hypertension complicating diabetes in pregnancy resulted in 100% mortality in this limited series of cases. Grade 2 arteriolar changes in toxemia of pregnancy associated with diabetes mellitus should warrant early termination of the pregnancy; if discovered in the first trimester, abortion may be indicated; if not noted until the third trimester, termination becomes necessary. If grade 3 or grade 4 eyeground changes develop during the first trimester, therapeutic abortion is probably indicated. When grade 3 or grade 4 eyeground changes are noted later, immediate interruption is necessary if the fetus is viable. The type and degree of the diabetes in this series does not seem to have as much effect on the fetal salvage as the type and severity of the toxemia.

Am. J. Roentgenol. & Rad. Therapy, Springfield, Ill.

67:891-1064 (June) 1952

The Leriche Syndrome (Thrombotic Obliteration of Aortic Bifurcation). D. Shapiro.—p. 891.
Roentgen Findings in Atelectasis of Newborn with Special Reference to Changes in Cardiac Silhouette. J. F. Martin and H. L. Friedell. —p. 905.
Position of Aortic Arch and Descending Aorta; Roentgenologic Signs in Childhood. R. Ash.—p. 924.
Separation of Blood Vessels From Walls of Lateral Ventricle in Rapidly Progressing Hydrocephalus. B. S. Epstein.—p. 929.
Carcinoma of Cardia of Stomach as Detected by Laminagraphy. R. L. Friedman and M. G. Wasch.—p. 932.
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Direct Irradiation of Carcinoma of Liver and Biliary Tract by Use of Radioactive Iodine (I^{131}) in Tetraiodophenolphthalein: Experimental and Clinical Study. G. H. Copher, V. H. Wallingford, W. G. Scott and others.—p. 964.
Effect of Total Body Roentgen Irradiation of Long Bones of Hamsters. B. M. Levy and R. Rugh.—p. 974.
Calculations for Distributed Sources of Beta Radiation. H. H. Rossi and R. H. Ellis Jr.—p. 980.
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Use of Roentgen Films in Dosimetry. G. D. Adams.—p. 991.
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American Surgeon, Atlanta, Ga.

18:637-734 (July) 1952

Fat Embolism. L. J. Levy.—p. 637.
Use of Streptokinase and Streptodornase in Injuries of Chest. H. A. Blake, W. H. Moncrief and J. H. Forsee.—p. 646.
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Pulmonary Adenomatosis and Its Relationship to Problem of Malignant Tumors of Lung. J. G. Strance.—p. 665.
Uterine Suspension; Indications and Status. W. H. Cave.—p. 670.
Repair of Massive Calvarial Defects. G. O. Dean and R. Watson.—p 678.
Partial Nephrectomy. C. A. Eberhart and R. Banks Jr.—p. 684.
Utilization of Aponeurosis Transversus Abdominis, Cooper's Ligament and Iliopubic Tract in Repair of Inguinal and Femoral Hernias. E. I. Hashimoto and J. H. Clark.—p. 690.
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Factors in Maternal Mortality in South Carolina. J. D. Guess.—p. 701.
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Annals of Surgery, Philadelphia

136:3-192 (July) 1952

Use of Paraffin as Aid in Obliterating Pleural Space Following Total Pneumonectomy. W. E. Adams and J. M. Fritz.—p. 18.
Surgical Aspects of Intrahepatic Biliary Obstruction. I. Aird.—p. 27.
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*Importance of Epidermoid Carcinoma in Situ in Histogenesis of Carcinoma of Lung. H. Black and L. V. Ackerman.—p. 44.
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Direct Cardiac Surgery in Treatment of Congenital Pulmonary Stenosis. R. C. Brock.—p. 63.
Persistence of Symptoms Following Cholecystectomy with Special Reference to Anomalies of Ampulla of Vater. W. G. Cole and W. J. Grove.—p. 73.
Surgery of Papillary Carcinoma of Thyroid Gland. C. Eckert and L. T. Byars.—p. 83.
*Mixed Tumors of Lung: Re-Appraisal. J. L. Ehrenhaft and N. A. Womack.—p. 90.
*Intracellular and Extracellular Potassium Deficits in Surgical Patients. R. Elman, B. A. Shatz, R. E. Keating and T. E. Weichselbaum. —p. 111.
Pulmonary Resection in Tuberculosis. J. W. Gale, H. A. Dickie and A. R. Curreri.—p. 132.
Recent Advances in Our Knowledge of Thyroid Gland. P. Heinbecker. —p. 145.
Motor Functions of Cat's Colon Following Excision of Auerbach's Plexus. F. W. Klinge.—p. 162.
Massive Melena. R. H. Moore.—p. 167.
Diaphragmatic Hernia. F. Nicholson.—p. 174.
Congenital Tumors of Spinal Cords in Infants. H. G. Schwartz.—p. 183.

Epidermoid Carcinoma in Situ of the Lung.—Black and Ackerman reviewed the microscopic sections in 60 recent cases of epidermoid and undifferentiated carcinoma of the lung removed at operation and found unquestionable carcinoma in situ in 13 and anaplastic hyperactivity of the intact bronchial epithelium in 8 other cases. In all of these cases the tumor was central in origin, arising in lobar bronchi or in one of their major segmental divisions. In addition, in all but 7 of the 60 cases, advanced squamous metaplasia of the bronchial epithelium was found. The microscopic sections were reviewed at random, and it is possible that more intensive search might reveal an even higher incidence of intraepithelial cancer. The authors list the criteria for identification of carcinoma in situ in the bronchus. If epidermoid carcinoma in situ is found in a bronchoscopic biopsy, three major possibilities are suggested: 1. The biopsy section represents an isolated single area of early cancer. 2. It is one of several similar areas of intraepithelial cancer. 3. The in situ carcinoma lies next to a frank invasive carcinoma. If the clinical factors such as history, radiological findings, and gross bronchoscopic appearance are in favor of the last possibility, the authors feel that one is justified in performing an exploratory thoracotomy without further confirmatory evidence. In cases in which biopsy reveals considerable basal cell hyperactivity and anaplasia, strong suspicion that a carcinoma is present should be entertained, and renewed efforts made to demonstrate its presence. In such cases the cytological examination of the sputum is of great value. In the 13 cases of carcinoma of the lung mentioned earlier in which epidermoid carcinoma in situ was associated, a positive cytological diagnosis was made in 10 cases, two were highly suspicious, and only one was negative. In this last case, only one sputum specimen and one bronchial washing had been examined. The authors conclude that

epidermoid carcinoma in situ may be present at the periphery of an invasive tumor or appear at multiple sites either in the same lung or in other portions of the tracheobronchial tree. The discovery of such a process almost invariably indicates an invasive tumor nearby and is an indication for an aggressive therapeutic approach.

Mixed Tumors of Lung.—Ehrenhaft and Womack point out that 13 years ago one of them, together with Graham, presented a study on mixed tumors of the lung on the basis of surgical specimens from relatively early lesions that had been treated by complete surgical extirpation. Little was known about these tumors, which were generally designated as adenomas of the bronchus, until the advent of bronchoscopic examination. The authors reasoned that these tumors, which were not infrequently seen during life but rarely during necropsy, did not disappear spontaneously, but rather changed their morphology as well as their clinical characteristics as they became invasive. Thus, at necropsy it would be difficult to differentiate them from bronchiogenic cancer. Such a concept would be in keeping with prototypes elsewhere in the body. Designating the tumor as adenoma of the bronchus is regarded as misleading by the authors, since in their experience it is an invasive lesion, which can and did metastasize, and at times it is not purely epithelial. The authors discuss 14 cases observed in recent years. The average age of these patients was somewhat younger than that of patients with squamous cancer of the bronchus, and, whereas squamous cancer is observed chiefly in men, mixed tumors seem to be somewhat more frequent in women. Physical examination of the chest reveals only those signs that are the result of bronchial obstruction. Where a major bronchus is involved, and this is the most frequent site, the instillation of iodized oil into the bronchus rarely fails to show occlusion. At such times bronchoscopic verification of the tumor is usually possible. The examination of the sputum for tumor cells has been disappointing. Since, in spite of early local invasion, distant metastasis is usually late, extirpative surgery frequently gives a good result. Since these tumors possess invasive characteristics, with a tendency to metastasize, they should be considered malignant growths in spite of the fact that many of them will persist for many years without dissemination. These tumors are composed of a mixture of different functioning tissues, and it is suggested that these lesions result from a failure of proper tissue coordination in pulmonary development.

Potassium Deficits in Surgical Patients.—Elman and associates attempt to draw a clearer picture of potassium deficits in surgical patients in terms of both intracellular as well as extracellular compartments. They review the literature and discuss four cases in which a detailed analysis was made. The authors stress the following points: 1. Potassium deficiency is commonly associated with persistent alkalosis and hypochloremia, which responds incompletely to administration of sodium chloride and/or ammonium chloride. Other clinical manifestations include signs and symptoms of muscular weakness and even paralysis, sensorial depression to coma, and instability of the peripheral circulation, especially to postural changes. 2. The plasma potassium and calcium levels are usually low in potassium deficiency and the low calcium may play a part in the pathogenesis of tetany and gastrointestinal hyperirritability. 3. Losses of potassium occur in the urine and in the gastrointestinal secretions, and tend to produce symptoms of potassium deficiency only when they exceed 200 to 400 mEq. (15 to 30 gm. of potassium chloride) in the average-sized adult. 4. To produce symptoms, such losses must be in excess of the potassium released by tissue protein breakdown when no protein is taken in, which can be calculated from the urinary nitrogen by using the ratio K/N= 2.9. 5. The amount of potassium required to correct intracellular deficits tends to be relatively small in patients who are in negative nitrogen balance due to excessive protein catabolism. In contrast, potassium deficient patients in positive nitrogen balance require relatively large amounts. 6. The kidney often loses 50% or more of the potassium given. Thus, twice as much must be administered as is actually deficient, i. e., about 400 to 1,000 mEq. (30 to 75 gm. of potassium chloride). 7. One of the methods to measure the intracellular deficit is the study of potassium balance. 8. Achievement of potassium balance requires up to 10 days of therapy. 9. Potassium administration is dangerous only when the plasma level is suddenly increased well above normal. This can be avoided by administering it in solution with a maximum concentration of 53 mEq. (4 gm. of potassium chloride) per liter. Greater concentrations tend to produce pain and phlebitis.

Annals of Western Medicine & Surgery, Los Angeles

6:399-466 (June) 1952

Indications for and Contraindications to Ovariectomy. J. C. Doyle. —p. 411.
Rehabilitation of Peripheral Nerve Injuries. J. H. Aldes, A. C. Bockstahler and L. I. Lieberman.—p. 418.
Betaine and Glycocyamine in Treatment of Disability Resulting from Acute Anterior Poliomyelitis. M. E. Borsook, H. K. Billig and J. G. Golseth.—p. 423.
Electrocardiographic Diagnosis of Myocardial Infarction in Presence of Bundle Branch Block. M. J. Kert.—p. 428.
Surgical Treatment of Post-Thrombotic Sequelae of Leg. R. L. Ross. —p. 431.
ACTH and Cortisone in Ophthalmology. S. R. Irvine.—p. 438.
Varicose Veins: Part VIII. Diagnostic Procedures. A. Fields.—p. 441.
Abdominal Distention and Gas Pains. W. H. Bachrach and L. Strauss. —p. 445.

Antibiotics & Chemotherapy, Washington, D. C.

2:281-334 (June) 1952

"Ilotycin," (Erythromycin) New Antibiotic. J. M. McGuire, R. I. Bunch, R. C. Anderson and others.—p. 281.
Ulceroglandular Tularemia Treated by Chloromycetin. N. M. Burleson and J. H. Miller.—p. 284.
Tolerance of Man for Isonicotinylhydrazines. R. A. Lewis.—p. 285.
*Effects of Aureomycin in Chronic Brucellosis. J. F. Griggs.—p. 290.
*Effects of Chloramphenicol in Chronic Brucellosis. J. F. Griggs.—p. 300.
Pleocidin, New Antibiotic Related to Streptothricin. J. Charney, W. S. Roberts and W. P. Fisher.—p. 307.
Physiological and Therapeutic Significance of Levo-Arterenol: Principal Hormone of Adrenal Medulla. A. M. Lands and M. L. Tainter. —p. 315.
Treatment of Canicola Fever with Chloramphenicol. D. Selman.—p. 329.

Aureomycin in Chronic Brucellosis.—This paper presents a study of 45 courses of aureomycin given to 34 patients with chronic brucellosis who have been followed for one to three years following treatment. The antibiotic was given by mouth. The mean dosage was 26.5 gm. of aureomycin in 21 days. Iodides were also given to all but eight patients and most patients received Brucella vaccine at some time in their history. Improvement resulted in three-fourths of all the patients and in 86% of those whose diagnosis had been considered certain. Extreme hypersensitization to Brucella was much improved by aureomycin. The patients with associated hypochondriasis had the least successful response to the drug. Relapse occurred after a few weeks or months either gradually or suddenly with the next intercurrent upper respiratory infection. Only four patients reported much improvement lasting more than six months. The relapse was often not so severe as before, especially in patients who were also desensitized with oxidized Brucella vaccine. Side-effects of the drug are common and unpleasant but not dangerous, and they can be mitigated. Aureomycin is a valuable adjunct in the treatment of most cases of chronic brucellosis, but it is not likely by itself to bring about a permanent arrest of the disease or even a very long remission.

Chloramphenicol in Chronic Brucellosis.—Twenty-five courses of chloramphenicol were given to 20 patients, 12 of whom had diagnoses of chronic brucellosis, 5 of probable chronic brucellosis, and three of possible chronic brucellosis. Clinical and symptomatic improvement resulted in half of the cases in each category. Side-effects of the antibiotic were prominent in more than half of the patients. Improvement or lack of improvement could not be correlated to the size of dose or duration of treatment. The duration of improvement resulting from chloramphenicol was limited to a few weeks or months. Any residual benefit lasting beyond six months may result from vaccine therapy as much as from chloramphenicol. The addition of iodides to the treatment produced no detectable benefit and may be a disadvantage. Chloramphenicol seems only of limited value in cases of chronic nonbacteremic brucellosis.

Archives of Physical Medicine, Chicago

33:327-376 (June) 1952. **Partial Index**

Mechanism of Absorption of Ultrasonic Energy in Blood. G. M. Piersol, H. P. Schwan, R. B. Pennell and E. L. Carstensen.—p. 327.
Prescribed Occupational Therapy. N. K. Covalt.—p. 333.
*Ineffectiveness of Ultraviolet Hemo-Irradiation in Distemper. K. G. Wakim, F. H. Krusen, C. F. Schlotthauer and F. R. Heilman.—p. 339.
Neuropsychiatric Aspects of Rehabilitation. F. G. Ebaugh.—p. 348.
Exercises Following Bankart Operation for Recurrent Shoulder Dislocation. J. L. Rudd and E. F. Haydock.—p. 353.
New Developments in Amputee Rehabilitation. A. Thomas.—p. 357.

Ineffectiveness of Ultraviolet Hemo-Irradiation.—The literature on ultraviolet irradiation of blood suggests that such therapy may be effective in the treatment not only of bacterial but also of virus infections. The consensus is that distemper is a virus disease characterized by an incubation period of three to six days. Thirty dogs stricken with distemper were used in this study; 15 were kept as controls while in 15 ultraviolet irradiation of the blood was carried out by the Knott procedure. This procedure was followed meticulously, and three important factors were kept strictly constant; (1) the amount of blood withdrawn and irradiated (1.5 cc. of blood per pound of body weight); (2) the time of exposure to ultraviolet energy; and (3) the intensity of ultraviolet radiation. At the end of 15 days, 11 of the 15 control dogs remained alive, while of the 15 dogs which were given ultraviolet irradiation of blood, only eight were still alive on the 15th day after treatment. Seven of the dogs given ultraviolet irradiation of blood died, while only 4 of the untreated controls died.

Arizona Medicine, Phoenix

9:1-72 (July) 1952

Adenoma of Islets of Langerhans: Case Report. M. C. Govostis, O. F. Bonnett Jr. and J. Van Prohaska.—p. 23.
Periodic Paralysis Associated with Exophthalmic Goiter. H. D. Cogswell and L. E. Beaton.—p. 26.
Sudden Deaths in Infants (with Reports of 4 Cases). J. Emmett and M. Rosenthal.—p. 29.
Letterer-Siwe Disease: Report of Case. R. H. Snapp.—p. 32.

Arkansas Medical Society Journal, Fort Smith

49:23-40 (July) 1952

Surgery of the Hand. K. G. Jones.—p. 23.
Report on Rural Health Conference of American Medical Association. M. G. Lawson.—p. 29.
Seasickness. R. L. Brier.—p. 31.

Blood, New York

7:577-670 (June) 1952

Acanthrocytosis: Genetic Erythrocytic Malformation. K. Singer, B. Fisher and M. A. Perlstein.—p. 577.
In Vitro Erythrophagocytosis in Acquired Hemolytic Anemia. W. H. Zinkham and L. K. Diamond.—p. 592.
Resistance of Reticulocytes and Young Erythrocytes to Action of Specific Hemolytic Serum. W. O. Cruz and P. C. Junqueira.—p. 602.
*Treatment of Paroxysmal Nocturnal Hemoglobinuria with ACTH. N. Kalant and D. P. Cyr.—p. 607.
Transfer of Myelogenous Leukemia Induced by Gastric Installation of Methylcholanthrene in Wistar Rats. H. Shay, M. Gruenstein, C. Harris and L. Glazer.—p. 613.
Leukopenia Following Administration of Nicotinic Acid. F. A. Bassen, A. D. Etess and R. L. Rosenthal.—p. 623.
*Hypersplenism: Case Report with Postmortem Study. B. A. Wiard and S. L. Robbins.—p. 631.
Vascular Factors in Pathogenesis of Hemorrhagic Syndromes. T. H. Spaet.—p. 641.

Corticotropin in Paroxysmal Nocturnal Hemoglobinuria.—Corticotropin was given a therapeutic trial in a man, aged 41, with paroxysmal nocturnal hemoglobinuria. Examination of the blood before the institution of corticotropin therapy revealed the following factors: a hemoglobin level of 5.6 gm. per 100 cc., 1,500,000 erythrocytes, hematocrit of 16%, 22% reticulocytes, and 62,000 platelets per cubic millimeter. Infusions of corticotropin solution intravenously were given for 11 days starting with 12.5 mg. per day, increasing to 80 mg., then decreasing to 10 mg., with a total of 437.5 mg. Each infusion was given over a period of 8 to 12 hours. In addition, the patient received five transfusions of washed red cells. Subjectively, there was a feeling of well-being, but there was no significant change in the color of the urine and the reticulocyte counts remained essentially at the pretreatment level. Three weeks after this initial failure a second intravenous course of 410 mg. of corticotropin given over 12 days, starting with 20 mg. daily, increased to 80 mg. and decreased to 5 mg., resulted in a dramatic deceleration of hemolysis. The decrease, however, lasted only five days after discontinuation of the therapy. A third attempt with a total of 790 mg. of corticotropin given intravenously over 17 days was again of no avail in relieving the condition. Treatment with bishydroxycoumarin (dicumarol®) coincided with a remission of the hemolysis, which has lasted, so far, for five weeks. Despite the brief period of improvement observed in this patient during corticotropin therapy, it would seem that corticotropin therapy should be added to the list of ineffectual methods of treatment of paroxysmal nocturnal hemoglobinuria.

Hypersplenism.—A case of hypersplenism giving rise to a panhematopenia is reported in a 57-year-old man. Splenectomy was refused, and the patient died six and a half months after diagnosis of Felty's syndrome had been made on the basis of the association of hypersplenism with rheumatoid arthritis. At necropsy pronounced phagocytosis of both red and white cells was noted in the spleen, supporting Doan's hypothesis that peripheral cytopenia is due to the mechanical removal of blood elements by a hyperactive spleen. There was in addition similar phagocytic activity throughout the entire reticuloendothelial system, including lymph nodes, liver, and bone marrow. The observation of complete maturation arrest of the white cell series of the bone marrow at the myelocytic level confirmed Dameshek's opinion, who suggested that splenic hyperfunction blocks normal marrow function. A third factor, to the best of the authors' knowledge never previously identified in cases of hypersplenism, was also present. This was a circulating substance that produced active lysis of normal white cells and must have contributed to the leukopenia. The anatomic observations in the authors' case suggest the possibility that generalized reticuloendothelial hyperfunction may be significant in the production of cytopenia in some patients with so-called hypersplenism.

Bulletin of Johns Hopkins Hospital, Baltimore

91:1-81 (July) 1952

Ultrafiltration Studies on Calcium and Phosphorus in Human Serum. T. Hopkins, J. E. Howard and H. Eisenberg.—p. 1.
Influence of Cortisone on Evolution of Acute Infection and Development of Immunity. F. G. Germuth Jr., B. Ottinger and J. Oyama.—p. 22.
*Hemorrhagic Disorder Occurring in Patients with Cyanotic Congenital Heart Disease. R. C. Hartmann.—p. 49.
Cholesterol Metabolizing Escherichia Coli: Preliminary Report. G. L. Curran and K. C. Brewster.—p. 68.

Hemorrhagic Disorder in Congenital Heart Disease.—Hartmann describes studies on 39 patients with cyanotic congenital heart disease, including 2 with fatal and 1 with serious postoperative bleeding. A surprisingly high incidence of potential hemorrhagic diathesis was found in the group with cyanotic congenital conditions. Impairment of clot retraction due to a combination of thrombocytopenia and low blood fibrinogen in the presence of a high hematocrit level was the most striking finding. The slight to moderate prolongation of the prothrombin time was clearly not the cause of the hemorrhagic disorder. Although hematological tests reveal potential hemorrhagic diathesis in all age groups, serious postoperative hemorrhage is chiefly a problem in adults and adolescents. When fatal hemorrhage occurred in children, it could usually be explained by local surgical causes. Children with marked abnormalities in their hematological tests had no hemorrhage at or following operation. One adult with severe impairment in hematological tests was subjected to phlebotomies and splenectomy prior to cardiac surgery. Subsequently a subclavian-pulmonary anastomosis was carried out without hemorrhage. The value of these procedures in preparing selected adults for cardiac surgery must be determined by further experience. Hartmann further suggests that use of anticoagulant drugs in cyanotic congenital heart disease may be dangerous.

California Medicine, San Francisco

76:367-416 (June) 1952

Physicians in Politics—as Good Citizens. L. A. Alesen.—p. 367.
Mechanism of Syncope and Action of Drugs in Complete Heart Block. M. H. Nathanson and H. Miller.—p. 370.
Avoiding Pitfalls in Urologic Diagnosis. H. M. Weyrauch.—p. 376.
Medical Group Practice in California. E. R. Weinerman.—p. 383.
*Conservative Amputation in Arteriosclerosis Obliterans. J. Flasher and H. B. Rubin.—p. 389.
Relationship of the Referring Physician to the Psychiatrist. D. Jackson. —p. 391.
Relationship of Delivery Date to Predicted Date. E. Liston.—p. 395.
Relation of Streptococcus to Epidemic Poliomyelitis: Studies in Etiology, Diagnosis and Specific Treatment. E. C. Rosenow.—p. 396.
Surgical Decompression of Bowel in Peritonitis. A. May and G. F. Norman.—p. 402.

77:1-120 (July) 1952

Rheumatoid Arthritis. Experiences with Hydrocortisone (Free Alcohol) and Hydrocortisone Acetate. E. W. Boland.—p. 1.
Management of Ureteral Stone: Guide for Physicians in General Practice. R. J. Prentiss, R. B. Mullenix and J. M. Whisenand.—p. 7.
Excision of Precancerous Lesions of Lip. H. L. Silvani and L. G. Brizzolara.—p. 12.
Effects of Creatine Precursors in Arthritis: Clinical and Metabolic Study of Glycocyamine and Betaine. A. R. Giggins, H. A. Harper, E. F. Kline and others.—p. 14.
Incidence of Poliomyelitis: Effect of Tonsillectomy and Other Operations On Nose and Throat. A. H. Miller.—p. 19.
Poliomyelitis and Parenteral Injections: Review of Recent Literature. R. M. Drake.—p. 22.
Possible Home Care in Poliomyelitis. M. Mills.—p. 29.
Small Hospital's Role in Poliomyelitis. E. B. Shaw and H E. Thelander. —p. 32.

Conservative Amputation in Arteriosclerosis. — Flasher and Rubin point out that McKittrick and co-workers recently reported encouraging results from transmetatarsal amputation in patients who had both arteriosclerosis obliterans and diabetes mellitus. They stated that patients who formerly would have been subjected to amputation of one or more toes or even of part of the leg received more benefit from the transmetatarsal operation. To appraise the conclusion reached by McKittrick and co-workers, a study was made of case records with a view to determining, first, how often and in what circumstances toe or leg amputation gave satisfactory results, and, second, whether transmetatarsal amputation might better have been considered. At Los Angeles County Hospital histories were reviewed of 49 unselected cases of patients with arteriosclerosis obliterans, some of whom had diabetes mellitus, upon whom amputation of a toe or toes or through the leg had been performed because of a lesion related to ischemia. A total of 63 amputations had been done on 57 limbs. In many cases in which toes were amputated, it was necessary later to amputate the leg or the thigh because of improper healing or spread of infection. Transmetatarsal amputations apparently heal frequently in carefully selected cases and permit better function in the foot than is possible after toe amputations. Successful use of a prosthesis is not obtained in many cases after leg amputation. When this difficulty is anticipated, transmetatarsal rather than leg amputation should be attempted, if other conditions warrant, since a prosthesis is not necessary after transmetatarsal amputation.

Florida Medical Association Journal, Jacksonville

39:1-72 (July) 1952

*Further Observations on New Concept of Baby Feeding. W. W. Sackett Jr. and B. J. Sheppard.—p. 21.
Prolapse of Gastric Mucosa into Duodenum: Report of Eight Cases. S. Stillman.—p. 25.
Incidence of Heart Disease in School Children of Pensacola, Florida. J. M. Packard, J. S. Graettinger and A. Graybiel.—p. 30.
Note on New Drugs, "Miracle" and Otherwise, for Tuberculosis. H. C. Sweany.—p. 37.
Allergy Survey of Florida in the Light of Present Knowledge. C. Bernstein and S. D. Klotz.—p. 38.

New Concept of Baby Feeding.—This paper describes further experiences with the new method of baby feeding, in which a six-hour feeding interval is used from birth. A trial of almost two years proved a degree of acceptance and workability beyond expectations. Clinical observations on the babies who had been put on the six-hour schedule revealed that in health, development, and general well-being they are on a par with those babies brought up on the more generally accepted theories of baby feeding. The main advantage in this schedule lies in the contribution to the mother's stability, which in turn is reflected in a baby who will present fewer feeding problems during the ensuing years of life. Furthermore, the mother can devote more time to other family obligations. The observations refute the ideas of modern child psychologists, who might be tempted to label babies fed on a six hour schedule as "thwarted individuals." On the contrary, the babies are happy and contented, in direct contrast to those babies fed on a demand schedule, who seem to develop constantly along "demanding lines."

Gastroenterology, Baltimore

21:185-330 (June) 1952

Effect of Psychoanalysis on Course of Peptic Ulcer: Preliminary Report. L. A. Stine and A. C. Ivy.—p. 185.
*Pseudomembranous Enterocolitis: Clinicopathologic Study of Fourteen Cases in Which the Disease Was Not Preceded by Operation. M. S. Kleckner Jr., J. A. Bargen and A. H. Baggenstoss.—p. 212.
Study of Diverticulitis of Colon in Office Practice. J. L. Horner.—p. 223.
Recurrent Jaundice in Chronic Relapsing Pancreatitis. S. Selesnick. —p. 230.
Primary Carcinoma of Liver: Critical Analysis of 16 Cases. F. W. Blatchford Jr.—p. 238.
Clinical and Experimental Value of Needle Biopsy of Liver. M. P. Tyor and D. Cayer.—p. 245.
Preliminary Evaluation of New Cholecystographic Medium "Telepaque." R. M. Lowman, H. W. Stanley, T. S. Evans and J. C. Mendillo. —p. 254.
Plasma Prothrombin in Viral Hepatitis and Hepatic Cirrhosis: Evaluation of Two Stage Method in 75 Cases. J. D. Mann.—p. 263.
Effect of Some Commonly Used Vasodilator and Sedative Substances upon Acidity and Volume of Gastric Juice. F. Steigmann, L. L. Hardt, S. Hyman and R. Schlesinger.—p. 271.
Effect of ACTH on Gastric Secretion in Experimental Animals. J. M. Zubiran, A. E. Kark and L. R. Dragstedt.—p. 276.
Action of Anthisan on Intestinal Secretion Produced by Histamine and Carbaminoylcholine. W. Koskowski and M. Mahfouz.—p. 280.
Effects of Alcohol on Secretion of Intestinal Juice and Activity of Invertase. W. Koskowski and M. Mahfouz.—p. 286.
Modification of Voegtlin Liver Biopsy Needle for Transthoracic Approach. R. S. Nelson.—p. 289.

Pseudomembranous Enterocolitis.—Acute pseudomembranous inflammation involving portions of the intestinal tract is found oftenest at necropsy, usually in patients who recently had undergone an intestinal operation. In order to determine the frequency of pseudomembraneous enterocolitis that is not preceded by an abdominal operation, Kleckner and associates of the Mayo Clinic reviewed the records of all cases in which necropsy was performed at the Mayo Clinic in the 11 years from 1940 to 1950, inclusive. The review revealed 14 cases of pseudomembranous enterocolitis of this type. In 7 of the 14 cases the pseudomembranous enterocolitis was considered the immediate cause of death. The following pathological conditions were associated with the pseudomembranous enterocolitis: obstruction of the large intestine in five cases, heart disease in five cases, and miscellaneous pathological conditions in four cases. In four of the five cases of obstruction of the large intestine the cause of the obstruction was carcinoma. Severe infection was present in three of the four cases in the miscellaneous group. The most significant clinical features were the sudden onset of profound circulatory collapse which was resistant to the usual supportive measures, and the presence of watery diarrhea, abdominal distention with features suggestive of paralytic ileus, and abdominal pain. All but one of the patients were more than 50 years of age. At necropsy, segments or long stretches of the small and large intestine had the mucosa covered or replaced by a gray, loosely adherent wrinkled, fibrinous membrane that contained necrotic cellular debris, leukocytes, and bacteria. The submucosa was edematous and hyperemic. The muscular coat usually appeared normal, but partial necrosis or inflammation occasionally was present in this layer.

Georgia Medical Association Journal, Atlanta

41:227-276 (June) 1952

Intestinal Obstruction in the Newborn Infant. C. M. Lee Jr.—p. 233.
Problems in Diagnosis of Bronchogenic Carcinoma. R. G. Ellison and J. L. Alexander.—p. 242.
Eye Lashes Embedded in Lens. M. B. Raiford.—p. 253.
Management of the Diabetic Patient. C. J. Wyatt Jr.—p. 255.
Therapeutic and Diagnostic Use of Procaine. H. S. Phillips and J. C Thoroughman.—p. 259.
Hysterectomy for Uncontrollable Postpartum Hemorrhage. W. W. Daniel. —p. 263.

Journal of Applied Physiology, Washington, D. C.

4:819-872 (May) 1952

*Alpha Content of Electroencephalogram in Relation to Movements Made in Sleep, and Effects of Sedative on This Type of Motility. M. A. B. Brazier and H. K. Beecher.—p. 819.

Effects of Atropine, Work and Heat on Heart Rate and Sweat Production in Man. F. N. Craig.—p. 826.

Mechanism of Exercise Proteinuria. N. B. Javitt and A. T. Miller Jr. —p. 834.

Thromboplastic Activity in Human Blood. A. J. Quick and E. Epstein. —p. 840.

Chylomicrons in Diabetics. E. S. Levy, S. C. Kraft and H. Necheles. —p. 848.

New Experimental Methods for Determination of Effective Alveolar Gas Composition and Respiratory Dead Space, in Anesthetized Dog and in Man. J. R. Pappenheimer, A. P. Fishman and L. M. Borrero. —p. 855.

Pulmonary Edema in Guinea Pigs During Severe Hypoxia. A. Hemingway.—p. 868.

Alpha Waves in Electroencephalogram in Movements During Sleep.—Of all the correlations that have been made between electroencephalographic changes and various conditions of the brain, one of the most consistent and striking is their correlation with the state of awareness of the patient. When there is loss of consciousness, as normally occurs in sleep, or abnormally as, for example, in coma, in anesthesia, in a faint, or in the stupor following an epileptic convulsion, the change in brain potentials is great. There have been many studies concerned with the arrival of sensory impulses at the cortex during these states of impaired consciousness, but little attention has been paid to the motor functions of the cortex. The authors decided to investigate the electroencephalogram during normal sleep with special reference to the occurrence of movements. The incidence of movements made when a normal subject is apparently asleep is usually high, and yet the presence of alpha activity in the brain potentials is very much reduced from that in the waking state. The authors were interested to see whether this paucity of alpha frequencies during sleep persisted when the subject made a movement, and whether a movement could in fact be initiated in the absence of an appreciable amount of alpha activity. Electroencephalograms were recorded throughout three hours of the night on nine normal subjects on each of two occasions. Quantitative measurements of the amount of alpha activity were made. In all the tests (with one exception) the mean of the alpha content in the period 10 to 0 seconds before a movement increased over that present in sleep. This trend towards wakefulness was found to have started in the period 20 to 10 seconds before the movement and to persist into the period 0 to 10 seconds after it. Using decrease in delta content as an additional index of increasing wakefulness, this was found to support the evidence for a decrease in depth of sleep preceding a movement. This change in level of sleep in the direction of wakefulness occurs irrespective of whether the sleep is natural or induced by sedatives (90 mg. sodium pentobarbital), but the administration of sodium pentobarbital (90 mg.) reduced the incidence of movements made during the three-hour sleep period (from a mean of 21 in normal sleep to a mean of 15). It would seem that the number of movements made during sleep can be used as an index of depth of sleep when testing drugs for their comparative hypnotic power.

Journal of Bacteriology, Baltimore

63:693-834 (June) 1952. **Partial Index**

Effect of Certain Acids of Tricarboxylic Acid Cycle on Growth of Escherichia Coli. B. C. Johnson and E. M. Cohn.—p. 735.

Activity of Catalase in Pasteurella Tularensis. Y. Avi-Dor and H. Yaniv. —p. 751.

Occurrence of B-Galactosidase in Escherichia Coli. G. Lester and D. M. Bonner.—p. 759.

Effect of Ultraviolet Irradiation on Gram Positiveness. J. W. Bartholomew and T. Mittwer.—p. 779.

Studies on Nutrition and Physiology of Pasteurella Pestis. I. Chemically Defined Culture Medium for Pasteurella Pestis. M. Rockenmacher, H. A. James and S. S. Elberg.—p. 785.

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Journal of Bone and Joint Surgery, Boston

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Bone Regeneration: Experimental Study of Bone-Grafting Materials. R. D. Ray, J. Degge, P. Gloyd and G. Mooney.—p. 638.

*Comminuted Fractures of Distal End of Radius Treated by Ulnar Pinning. A. F. DePalma.—p. 651.

Dislocation of Tibiotalar Joint Without Fracture: Unusual Ski Injury. M. P. Fonda.—p. 662.

*The Infant's Persistent Thumb-Clutched Hand. J. W. White and W. E. Jensen.—p. 680.

Chondromalacia Fabellae. R. R. Goldenberg and E. L. Wild.—p. 688.

Periosteal Chondroma: Distinctive Benign Cartilage Tumor. L. Lichtenstein and J. E. Hall.—p. 691.

Rupture of Extensor Digitorum Communis Tendons Following Severely Deforming Fractures About the Wrist. H. Gladstone.—p. 698.

Ulnar Pinning in Comminuted Fractures of Distal End of Radius.—Fractures of the distal end of the radius are the commonest fractures encountered, but there is need of studies to determine whether or not present methods of management are adequate. Loss of length of the radius, diminution or obliteration of the radial tilt of the articular surface of the radius, and supination of the distal segment of the radius are the three factors chiefly responsible for poor cosmetic and functional results. The method of treatment described here was first suggested by Briggs. It consists in reduction of the fracture by traction and molding of the fragments. The corrected position is maintained by means of a threaded wire passed through the ulna to the most distal radial fragment, which invariably includes the styloid process of the radius. It was reserved for patients with comminution of the articular surface of the radius. Twenty-eight of the 39 patients treated by this means have had a follow-up period of from 12 to 36 months. No infection occurred when a threaded wire was used and cut below the level of the skin. In two cases in which an unthreaded wire was used and the wire left protruding from the skin, a low-grade infection developed around the pin site but subsided on removal of the pins. The author concludes that this method of ulnar pinning after reduction by traction and manipulation, in which all components of the fracture are corrected, has yielded a satisfactory percentage of excellent and good results.

Thumb Deformities in Infants.—Eight cases of aplasia or hypoplasia of hand tendons are presented. The resultant deformity consists in flexion of the thumb into the palm of the hand. The first metacarpal is held in abduction and the proximal phalanx is flexed forward and partially subluxated. Ulnar deviation of the hand is also frequently present. In the first patient treatment with splinting was begun when the boy was about 5 weeks old and was continued for seven months. The tendon anomaly was then recognized, and several months later, the extensor communis indicis tendon was transferred to the base of the proximal phalanx of the right thumb. A similar procedure was carried out on the left hand. Both thumbs were held in a plaster cast for four weeks, after which an elastic splint was used. Six weeks after operation there was already evidence of some extensor action. In an older sister of this boy, all fingers were held in a position of flexion. She was given pads and splints, and stretching exercises were advised; this improved all of the fingers except the thumbs. On the assumption that the pathological condition was in the soft tissues on the flexor surface of the thumb, a tenotomy of the flexor pollicis brevis and a full-thickness graft to the flexor aspect of the right thumb was performed when she was about two and one-half years old, and she wore a splint for about seven months without success. Then the common extensor of the index finger was transferred to the

base of the proximal phalanx of the thumb. Function of this transplanted tendon slowly developed and ultimate good function is expected. The third patient, besides thumb deformities, had a calcaneovalgus deformity of both feet. The mother of this child and two of her sisters also had deformities. In the seventh patient, the grandparents and a sister also had thumb deformities or tendon anomalies of the hands. The eighth patient, besides having hand deformities, also had bilateral clubfoot. Evaluation and interpretation of tendon malformation in infants and small children is difficult. The results of the tendon transplantations will take a few years to evaluate, although the early results have been encouraging. Some tendons may be hypoplastic or rudimentary, and it is felt that with proper splinting and exercises they can be strengthened without surgery. If a tendon is absent or if there is marked deformity and no response to conservative treatment, some form of tendon transplantation is indicated.

Journal of Experimental Medicine, New York

96:1-106 (July) 1952

Studies on Hemagglutination and Hemolysis by Escherichia Coli Antisera. E. Neter, L. F. Bertram, D. A. Zak and others.—p. 1.
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Homotypic Complement-Fixing Antibody in Monkeys Infected with Type 2, Poliomyelitis Virus by Oral Route. J. Casals, P. K. Olitsky and A. B. Sabin.—p. 55.
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Preparation and Properties of Type-Specific M Antigen Isolated from Group A, Type 1 Hemolytic Streptococcus. R. C. Lancefield and G. E. Perlmann.—p. 71.
Preparation and Properties of Protein (R Antigen) Occurring in Streptococci of Group A, Type 28 and in Certain Streptococci of Other Serological Groups. R. C. Lancefield and G. E. Perlmann.—p. 83.
Transitory Appearance of Type 2 Neutralizing Antibody in Patients Infected with Type 1 Poliomyelitis Virus. A. B. Sabin.—p. 99.

Journal of Investigative Dermatology, Baltimore

18:419-490 (June) 1952. **Partial Index**

Treatment of Monilia (Candida Albicans) Infections with Carbowax-Sulfur Ointment. (Preliminary Report). J. G. Hopkins, J. T. Weld and B. M. Kesten.—p. 419.
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Journal Lab. and Clinical Medicine, St. Louis

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Effects of Cortisone on Cutaneous Histamine Response of Rabbits Using Evans Blue Dye as Indicator. J. W. Chappell, R. H. Ebert and W. R. Barclay.—p 896.
Effects and Clinical Significance of Bacterial Contaminants in Transfused Blood. A. I. Braude, J. P. Sanford, J. E. Bartlett and O. T. Mallery Jr.—p. 902.
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J. Pharmacology & Exper. Therap., Baltimore

105:109-252 (June) 1952. **Partial Index**

Analgesic Potency and Side Action Liability in Man of Heptazone, WIN 1161-2, 6-Methyl Dihydromorphine, Metopon, Levo-Isomethadone and Pentobarbital Sodium, as Further Effort to Refine Methods of Evaluation of Analgesic Drugs. A. S. Keats and H. K. Beecher.—p. 109.
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Effect of Subnauseant Doses of Syrup of Ipecac on Gastric Acidity and Activity. W. D. Hagamen, C. M. Berry and S. Wolf.—p. 240.
Effect of Chloramphenicol and Certain Other Drugs on Oxidation of Aromatic Amino Acids by Strain of Pseudomonas Aeruginosa. F. Bernheim and W. E. DeTurk.—p. 246.

Journal of Thoracic Surgery, St. Louis

23:539-648 (June) 1952

Perivascular Space of Pulmonary Vessels: Anatomic Demonstration. A. M. Tocker and H. T. Langston.—p. 539.
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Spontaneous Hemopneumothorax. C. A. Ross.—p. 582.
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Surgical Treatment of Post-Thoracoplasty Painful Back. L. M. Shefts. —p. 602.
Limited Thoracoplasties with Extrafascial Apicolysis. W. R. Sweetman. —p. 611.
*Pulmonary Resection for Tuberculosis. E. B. Sive, E. Bogen and F. S. Dolley.—p. 619.
Six-Fingered Glove for Mitral Commissurotomy. E. R. Munnell.—p. 628.

24:1-104 (July) 1952

The Waste of Slaughter and the Rage of Fight. F. B. Berry.—p. 1.
Fibrosarcoma of Bronchus: Report of Three Cases Diagnosed by Bronchoscopy and Treated by Resection. C. F. Storey.—p. 16.
Mercury-Bag Bolus to Expedite Passage of Esophageal Dilator Guide String. F. H. Aves, G. Desforges and J. W. Strieder.—p. 34.
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Carcinoma of Esophagus Complicating Cardiospasm: Report of Case. I. Gore and C. R. Lam.—p. 43.
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Indications for Delayed Roentgenogram in Bronchography. I. J. Kane and S. Heiser.—p. 70.
Atresia of Cervical Esophagus. E. K. Johnson and J. L. Mangiardi. —p. 75.
Effects of Increased Endobronchial Pressure, Vitamin A Deficient Diets, and Nasopharyngeal Installations of Bacteria on Tracheobronchial Trees of Young Rats. J. F. O'Neill, H. H. Bradshaw, F. Hightower and D. E. Ward Jr.—p. 80.
Trans-Sternal Tracheal Excision for Carcinoma: Report of Case. G. R. Minor.—p. 88.
Endobronchial Carcinosarcoma. H. E. Taylor and M. V. Rae.—p. 93.
Wound of Superior Vena Cava with Survival. T. R. Hudson.—p. 101.

Pulmonary Resection for Pulmonary Tuberculosis.—Sive and associates say that before the introduction of streptomycin, pulmonary resection for tuberculosis was done at their hospital only occasionally. As a rule, resection was reserved for cases in which nothing else could be done, because with the old tourniquet method and without the aid of streptomycin, bronchopleural fistula and empyema were rather frequent and the surgical mortality was high. During the last four years, however, resection has been done more frequently. The authors review 84 cases in which pulmonary resection was done for tuberculosis by the individual ligation technique. Nine of the patients died. Follow-up examinations from one to four years later on the 75 who survived showed 60 with negative sputum, of whom 23 had been able to resume their occupation. The results were least favorable in the Negro race, patients with large or tension

cavities, and in those already resistant to streptomycin. Poor results were also noted in patients in whom the disease spread postoperatively and in those who required more chemotherapy or postresection thoracoplasty. Pulmonary resection is a valuable therapeutic measure in selected cases of pulmonary tuberculosis, especially for lesions that have not been controlled by thoracoplasty.

Kentucky State Medical Assn. Journal, Bowling Green

50:227-266 (June) 1950

Doctors Are Citizens, Too. R. B. Chrisman.—p. 227.
Relapsing Pancreatitis. E. E. Gambill.—p. 230.
Tropical Diseases in the Southwest Pacific Area. D. M. Kuhns.—p. 235.
Management of Severe Allergic Bronchial Asthma. M. Kaufmann. —p. 247.

50:267-316 (July) 1952

Cortisone and ACTH in Treatment of Chronic Arthritis. R. L. Cecil. —p. 267.
Some Encouragements in Cancer Surgery. F. W. Rankin.—p. 274.
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Diagnosis and Treatment of Aneurysms and Arteriovenous Fistula. D. C. Elkin.—p. 289.
Torular Meningo-Encephalitis. T. M. Marshall.—p. 292.

Maine Medical Association Journal, Portland

43:169-228 (June) 1952

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Lupus Erythematosus Disseminatus: Report of Case in a Male. C. W. Morris.—p. 174.
Acute Tuberculous Pericarditis: Report of Case. J. B. Dana.—p. 180.
Gastroscopy: Important Diagnostic Procedure. R. G. Metcalf and D. H. Daniels.—p. 185.

Maryland State Medical Journal, Baltimore

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SYMPOSIUM ON THE DOCTOR IN COURT

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Expert Testimony from Viewpoint of the Jurist. W. C. Smith.—p. 288.
Abscess of Lung Due to Endamoeba Histolytica Treated by Surgery and Aureomycin. M. Ginsberg and J. M. Miller.—p. 295.

Missouri State Medical Assn. Journal, St. Louis

49:533-636 (July) 1952

Management of Fractures of Patella. C. R. Rountree.—p. 549.
Clinical Experience with Urokon Sodium 30 Per Cent (pH 7) for Cerebral Arteriography. W. B. Seaman and H. G. Schwartz.—p. 553.
Renal Failure. F. U. Steinberg.—p. 557.
*Surgical Treatment of Hematemesis Due to Esophageal Varices from Portal Cirrhosis by Ligation of Hepatic and Splenic Arteries. P. A. Knepper, L. W. Ide, R. V. Riddell and J. R. McDaniel.—p. 563.

Surgical Treatment of Hematemesis Due to Portal Cirrhosis.—The occurrence of portal cirrhosis with multiple episodes of hematemesis due to esophageal varices is reported in a 37-year-old woman. Surgical intervention was considered necessary for the survival of the patient because of the prospect of more hemorrhages. At laparotomy the liver was observed to be cirrhotic with multiple areas of regeneration of tissue. The pressure in the portal system was found to be 32 cm. of water. The hepatic artery was approached through the gastrohepatic ligament and isolated between the site of its origin from the celiac axis and the point where the gastroduodenal artery arises. A bulldog clamp was applied at this location. The splenic artery was approached through the gastrocolic ligament and isolated near the spleen, where a bulldog clamp was placed. Another determination of the pressure in the portal system revealed it to be 18 cm. of water. A double ligation of each vessel in continuity with silk was then done where the clamps had been applied. Postoperative studies suggested that no liver damage resulted from the procedure. Seven weeks after surgery the patient had no symptoms, there was no roentgenologic evidence of esophageal varices, and the patient was carrying out her household activities. The relatively short follow-up necessitates a cautious prognosis in regard to further episodes of hematemesis. The author's case was considered to belong to Blakemore's group 2 of patients in whom the liver function is adequate to furnish the required amount of albumin and prothrombin, but as a result of fibrotic contractions and periportal fibrosis a severe degree of portal hypertension has supervened. Portacaval shunt operations were advised in this group. The same type of selectivity in choosing patients for hepatic and splenic arterial ligations appears to be useful.

Nebraska State Medical Journal, Lincoln

37:205-240 (July) 1952

Presidential Address. D. B. Steenburg.—p. 207.
Management of Acute Low Back Problems. C. H. Waters Jr.—p. 209.
How to Keep Our Liberty. R. Moley.—p. 213.
Electrocardiographic Transmission Over Standard Telephone Lines. W. E. Rahm Jr., J. L. Barmore and F. L. Dunn.—p. 222.

New England Journal of Medicine, Boston

246:951-992 (June 19) 1952

Role of Research in Modern Voluntary Teaching Hospital. O. H. Wangensteen.—p. 951.
Systolic Expansion of Left Auricle in Mitral Regurgitation. M. Elkin, M. C. Sosman, D. E. Harken and L. Dexter.—p. 958.
*Cortisone as Adjunct to Chloramphenicol in Treatment of Rocky Mountain Spotted Fever. J. B. Workman, J. A. Hightower, F. J. Borges and others.—p. 962.
Abdominal Surgery. C. E. Welch.—p. 967.
Vitamin A Intoxication: Report of Case. G. C. Reyersbach, J. Hanelin and R. J. Joplin.—p. 978.
Charles Scott Sherrington, 1857-1952: An Appreciation. H. R. Viets. —p. 981.

Cortisone and Chloramphenicol in Rocky Mountain Spotted Fever.—A therapeutic trial of cortisone combined with chloramphenicol (chloromycetin®) was carried out in four adults and five children with Rocky Mountain spotted fever. Chloramphenicol, in 250 mg. capsules, was administered orally in a total daily dose of approximately 50 mg. per kilogram of body weight. Adults received 3 gm. initially and 1 gm. every eight hours until they were afebrile for at least 48 hours; children were given about two-thirds the adult dose. Cortisone, in 25 mg. tablets, was given orally to three patients, and cortisone acetate suspension (25 mg per cubic centimeter) was given intramuscularly to the remaining six patients. Adults received an initial dose of 200 mg. followed by two doses of 100 mg. each, at six hour intervals; children were given approximately two-thirds the adult dose. In all patients, the total duration of cortisone therapy did not exceed 12 hours. Therapy was begun on the 4th to 13th day of the disease. Clinical improvement was uniformly observed within 24 hours or less after the institution of combined therapy. The most striking observations were alleviation of headache, dissipation of the toxic state, and return of appetite. There were no deaths. Results suggested that the combination of cortisone with chloramphenicol significantly enhanced amelioration of the signs and symptoms of Rocky Mountain spotted fever. These findings warrant additional clinical testing, particularly in the severely ill patients first observed late in the course of their disease.

246:993-1024 (June 26) 1952

Ureteral Complications and Alterations of Ureteral Tonus in Regional Ileitis. M. H. Redish.—p. 993.
Fungous Disease in Man Acquired From Cattle and Horses. (Due to Trichophyton Faviforme). O. F. Jillson and W. R. Buckley.—p. 996.
*Comparison of Duration of Action of Various Long-Acting ACTH Preparations in Human Subjects. W. Q. Wolfson and S. S. Fajans.—p. 1000.
Chiari's Disease—Hepatic-Vein Thrombosis: Report of Case. A. P. Caputi and T. A. Warthin.—p. 1004.
Medical Progress. Objectives and Limitations of Orthodontic Therapy. L. T. Swanson.—p. 1007.
Acute Calcific Tendinitis and "Frozen Shoulder": Their Treatment with ACTH. T. B. Quigley and A. E. Renold.—p. 1012.

Long-Acting Corticotropin Preparations.—The following preparations were studied: 1. "Adactar," which is a suspension of aluminum-phosphate-adsorbed corticotropin in polyvinyl pyrrolidone. Satisfactory preparations could be made in either of two ways. In the "triple-mix" method a sterile suspension of colloidal aluminum phosphate was added to sterile corticotropin powder and, after adsorption was complete, sterile polyvinyl pyrrolidone was added. In the "single-mix" method, a sterile solution of corticotropin in 60 to 90% propylene glycol was

added to a premixed diluent ("adactar vehicle 40") containing suitable amounts of colloidal aluminum phosphate and polyvinyl pyrrolidone. 2. "Adactar" tannate is identical with "adactar" prepared by the "single-mix" technique, except that corticotropin tannate solutions were used in its preparation. In both "adactar" and "adactar" tannate, the aluminum-phosphate concentration varied from 10 to 20 mg. per cubic centimeter, and the polyvinyl pyrrolidone concentration varied from 25 to 30%. The corticotropin concentration (in terms of the U.S.P. standard) was either 20 or 40 units per cubic centimeter in all long-acting preparations studied. 3. "Acthar-in-oil" ("adactar-0-40") is a suspension of corticotropin in peanut oil and 3% aluminum monostearate. 4. Corticotropin in gelatin includes two types of preparations, both made from heavy gelatin and both solid at room temperature. One material (designated ANG-H) was processed from nonhydrolyzed, neutralized, nonantigenic gelatin. The second material (designated ADDR-H-T) was made from partly hydrolyzed neutralized nonantigenic gelatin; in this preparation, corticotropin tannate rather than corticotropin was used. It was found that a rapid evaluation of the duration of action of different long-acting corticotropin preparations may be obtained by comparing their ability to induce a decrease in blood eosinophils that persists for 24 hours after a single 100-unit dose. Subjects must not receive exogenous corticotropin or cortisone in other forms at the same time. In 97 such assay studies, no patient had an undesirable systemic or psychological response to the single 100-unit dose of long-acting corticotropin. This method of analysis has been applied to four long-acting corticotropin preparations. "Adactar" and "adactar" tannate have a duration of action superior to that of either "acthar-in-oil" or corticotropin in heavy gelatin. Results with "adactar" were almost identical to those obtained with "adactar" tannate. Results with corticotropin in gelatin were slightly superior to those obtained with "acthar-in-oil." Selection of a long-acting corticotropin preparation for general clinical use cannot be made on the basis of duration of action alone. Such factors as temperature stability, ease of administration, and tendency to cause local or systemic reactions, should also be considered.

247:1-38 (July 3) 1952

Serial Courses of Corticotrophin or Cortisone in Chronic Bronchial Asthma. R. P. McCombs.—p. 1.
Sudden Blindness Due to Intracranial Vascular Accident: Simultaneous Bilateral Homonymous Hemianopia (Without Sparing of Macula) Following Infarction of Visual Cortex. O. H. Wagman.—p. 7.
*Cushing's Syndrome Treated by Removal of Adrenal-Cortex Tumor. F. L. Nichols, S. A. Root, C. S. Mirabile and R. S. Lampson.—p. 11.
Studies on Mutual Effect of Suboptimal Oral Doses of Vitamin B_{12} and Folic Acid in Pernicious Anemia. E. H. Reisner Jr. and L. Weiner.—p. 15.
Surgery of Heart and Great Vessels. R. H. Sweet and J. G. Scannell.—p. 18.

Cushing's Syndrome Treated by Removal of Adrenal Cortex Tumor.—Cushing's syndrome may result from any one of several causes, but the common denominator is the overproduction of adrenal cortical hormones with their typical effects on sexuality, electrolytes, and carbohydrate metabolism. Cushing's syndrome may originate in the adrenal cortex, due to either tumor or hyperplasia. In the case reported here the picture of Cushing's syndrome was unusually complete. An adrenal tumor weighing 1,840 gm. was successfully removed by the transthoracic approach, and the patient is steadily improving 26 months after operation. Adrenal cortex adenomas resemble grade 1 carcinomas histologically and can only be differentiated by the absence of tumor cells outside the gland. In the case here reported the prognosis is still guarded, although the tumor seemed well encapsulated and removal was apparently complete, and there has been no return of signs or symptoms of adrenal hyperfunction. Most of the preoperative signs and symptoms shown by this patient could be ascribed to one or the other of the cortical steroids. The psychiatric aspect of the syndrome is important. These patients show depression and seclusiveness because the changes in their appearance occur so rapidly that close friends may fail to recognize them. Suicidal tendencies may appear. Feelings of hopelessness persist in the postoperative period, and they are irritable and emotional. It is of interest that with the loss of excess cortical hormone the patient described first had flushes and then mild rheumatoid arthritis of her fingers.

New York State Journal of Medicine, New York

52:1393-1468 (June 1) 1952

Therapy of Idiopathic Orolingual Paresthesias. A. H. Kutscher, H. F. Silvers, G. Stein and others.—p. 1401.
Psychosomatic Approach to Sinus Headache. C. K. Gale.—p. 1406.
Comparative Study of Exercise, Anoxemia, and Ergonovine Tests for Coronary Insufficiency. I. Stein, J. Weinstein, J. J. Weiss and S. R. Slater.—p. 1409.
Role of Efocaine in Anorectal Anesthesia and Analgesia. J. M. Gross and H. E. Shaftel.—p. 1413.
Disseminated Lupus Erythematosus in the Negro. L. Rosenbaum and T. Cohen.—p. 1418.
*Effect of Antibiotic Drugs on Blood Clotting: Clinical Observations and Résumé of Recent Literature. M. A. Miller and H. E. Bass.—p. 1423.
Splenectomy in Two Chinese Siblings with Mediterranean Anemia. I. Shapiro, H. Schneck and A. D. Etess.—p. 1426.

Antibiotic Drugs and Blood Clotting.—The belief that antibiotic therapy encourages thromboembolism is rather widespread. In order to determine whether antibiotic therapy influenced the results of determinations of prothrombin time, bleeding time, clotting time, and platelet count, these laboratory determinations were made on eight patients who received therapeutically effective amounts of penicillin, streptomycin, chloramphenicol (chloromycetin®), and aureomycin, singly or in combination. The average daily dose was 600,000 units of penicillin, 2 gm. of streptomycin, and 3 gm. of chloramphenicol or aureomycin. They did not have blood dyscrasias or other conditions that might have influenced the laboratory tests under investigation. There was no change in the platelet count, bleeding time, or clotting time of any patient. In six patients no change was found in the prothrombin time. In two patients an increase in prothrombin time occurred after the sixth day of treatment.

Pennsylvania Medical Journal, Harrisburg

55:529-624 (June) 1952

*Shoulder Disabilities Associated with Coronary Disease. J. V. Cady.—p. 549.
Cancer in Infancy and Childhood. J. B. Arey.—p. 553.
Analgesia and Anesthesia in Obstetrics. G. J. Thomas.—p. 558.
Treatment of Nephrosis in Children. L. Greenman and T. S. Danowski.—p. 563.
The Normal and Abnormal Personality. M. W. Brody and H. F. Stochen.—p. 567.

Shoulder Disabilities Associated with Coronary Disease.—The association of painful dystrophies and other disabilities of the shoulder or hand, or both, with coronary disease is not only a definite entity but too frequent to be coincidental. Of 26 men and 8 women with the so-called shoulder-hand syndrome reported on by the author, 18 had had well-documented myocardial infarctions and 16 had suffered recurrent attacks of angina pectoris. Various theories have been proposed to explain the mechanism of this disability of the upper extremities, and Ernstene's concept that certain patients with severe coronary pain may keep the muscles of the shoulder girdle on one or both sides in a state of abnormal tension as a protective mechanism against the possible recurrence of pain seems to be the most practical. The syndrome is most likely to develop in patients whose arm and shoulder motion is restricted for one reason or another. Of the author's 34 patients, all except 6 admitted periods of immobilization of the shoulder or arm, or both, either instituted by themselves or by friends or by attending physicians. The author would strongly recommend the opposite type of advice, namely, that the patient under treatment for myocardial infarction or severe angina pectoris use his arms much more freely than he is customarily permitted to do. According to this point of view, treatment of 31 of the 34 patients depended solely on physiotherapy consisting of vigorous active exercises that required forced rotation and extension of the shoulder joints, as well as forearm and hand exercises, which were executed hourly by the patients while awake. Based entirely on the patient's evaluation, results at the end of a 18.2 months follow-up period were excellent in 21, good in 10, and fair in 3. Physiotherapy has not totally overcome the nodulations and contractures of the palmar aponeuroses, and is of greatest benefit when only the shoulder is involved. But even in cases of hand involvement, provided that contracture did not approach a clawhand, there has been a distinct decrease of swelling and pain and increased motility.

Psychoanalytic Review, Albany, N. Y.

39:115-212 (April) 1952

Psychoanalysis and Autonomic Nervous System: Bioanalytic Approach to Problem of Psychogenesis of Somatic Change. T. S. Szasz.—p. 115.
Psychoanalytic Study of Migraine and Psychogenic Headache. M. Sperling.—p. 152.
He Murdered to Get Hanged: Pre-Analytical Case History of 1783. W. Eliasberg.—p. 164.
Psychonomic Principle in Human Behavior. B. Karpman.—p. 168.

Rocky Mountain Medical Journal, Denver

49:479-560 (June) 1952

Presidential Address. C. S. Stone.—p. 501.
Senility and Senescence in Ophthalmology. E. B. Spaeth.—p. 506.
Bilateral Cortical Necrosis of Kidney. A. J. McQueeney and H. K. Speed Jr.—p. 513.
Effect on Morbidity of Abdominal Surgical Wounds Managed Without Postoperative Dressings: Review of 200 Cases. O. J. Rojo and J. R. Pratt.—p. 516.

Tennessee State Medical Assn. Journal, Nashville

45:221-262 (June) 1952

Office Treatment of Gynecological Disorders. H. E. Jones.—p. 221.
Office Management of the Diabetic Patient. P. K. Bondy.—p. 227.
Homografts of Fetal Membranes as Covering for Large Wounds—Especially Those from Burns: Experimental and Clinical Study (Preliminary Report). B. Douglas.—p. 230.
Nature of Obstruction About Bladder Neck. J. Dougherty.—p. 236.

Virginia Medical Monthly, Richmond

79:351-418 (July) 1952

*Edema and Lymphedema of Lower Extremities. E. L. Lowenberg.—p. 351.
*Subtypes of Migraine. F. V. Vance Jr. and W. O. Klingman.—p. 363.
Steroid Hormones and Rheumatism: Report of Two Cases of Rheumatoid Arthritis. J. S. Davis Jr. and H. Bartfeld.—p. 367.
Acute Porphyria and One False Initial Diagnosis Due to Previous Taking of Pyridium. T. E. Stanley, P. E. Schools and H. Field Jr.—p. 371.
How Young Am I? A. L. Chapman.—p. 375.
Gastric Surgery in Small Hospital. J. M. Emmett and G. R. Clutts.—p. 380.
Review of Present Concepts on Autonomic Control to Gastrointestinal Viscera: Clinical Applications. K. Plummer.—p. 385.
Basal Cell Epithelioma in Childhood. C. S. Lingamfelter and C. E. Wheeler.—p. 389.
Results of Subtotal Gastric Resection for Peptic Ulcer. M. K. King.—p. 391.
Clinicopathological Reports: From Case Records of Medical College of Virginia and University of Virginia Hospitals. H. Walker and W. Kay.—p. 394.

Edema and Lymphedema of Lower Extremities.—Edema and lymphedema are defined, and the present status of knowledge of these conditions is reviewed. All acutely edematous legs should be treated energetically from the onset. Eradication of varicosities will relieve only the mildest cases of associated edema. When considerable edema exists, vein ligation and stripping should be accompanied by a Kondoleon procedure (excision of fascia) on the lower leg. The patient with lymphedema praecox treated nonsurgically must wear a strong elastic support. The lymphatic system of the lower extremities has almost no reserve capacity and readily becomes decompensated. Measures that act as lymphagogue or tend to restore lymphatic compensation are elevation, compression, exercise, massage, restriction of salt and water, and vigorous diuresis. Diuresis is a true and powerful lymphagogue, not merely a dehydrating process. Mild, unexplained lymphedema in women may be secondary to cervicitis. Ascending infection of the pelvic lymph nodes causes central lymphatic obstruction of the lymphatics of the leg. In such instances, treating the cervix may cure the lymphedema. Vigorous anticoagulant therapy is an essential part of the treatment of all types of inflammatory lymphedema, to limit the destruction by thrombosis of the lymphatic channels. Acute allergic lymphedema responds well to corticotropin and cortisone. The leg swelling of acute iliofemoral thrombophlebitis is lymphedematous. The mainstays of treatment are anticoagulant therapy and paravertebral blocks of the lumbar sympathetic ganglions. Prolonged bed rest is contraindicated. Penicillin has no value. Lumbar sympathectomy is of limited value in chronic lymphedema. Simple paravertebral procaine (novocaine®) blocks will do as much for the leg swelling, but lumbar sympathectomy is indicated for causalgia, excessive perspiration, and ischemia. When chronic inflammatory lymphedema has produced the "indurated leg," only surgical measures will help. At the author's clinic several types of composite one-stage operations are done; most of them have as their basis the removal of all abnormal skin, subcutaneous tissue, fascia, the simultaneous correction of existing venous abnormalities, and the resurfacing of the leg with normal skin on normal muscle.

Subtypes of Migraine.—The recurrent type of headache generally referred to as migraine is apt to appear in several members of a family, is frequently preceded by visual disturbances, and is accompanied by nausea and vomiting. Symptomatic departures from classical migraine exist but frequently are not recognized as part of the migraine syndrome. Many cases are detected only if specifically inquired about in obtaining the history in cases of recurrent headache. In doing this the authors found that these variants or equivalents of migraine are almost as common as the conventional type. The common type of migraine is that in which there is vasospasm or vasodilating phenomena progressing from the occipital lobe with scotoma, flashings of light, or revolving circles. If this same type of disturbance of function arises in other areas of the brain, for instance, if vasospasm or dilation involves the parietal lobe, there will be a prodrome or an aura in which the first manifestation is not visual but is one of subjective sensory disturbances, frequently about the face, cheek, or in the fingers. The conventional pattern then follows in which the sensory disturbance may extend or may remain localized, then subsides and after a short free interval of 20 to 45 minutes is followed by typical hemicrania, nausea, and vomiting. In other instances the motor area is involved, with resulting transient paralysis, usually of an arm, lower face, or even complete hemiplegia. When areas for specialized functions are involved, such as consciousness, speech, motor skill, taste, hearing, or coordination, a wide variety of confusing symptoms and signs can appear. When ophthalmoplegia occurs as the preliminary or preheadache phenomenon, the disturbances implicate the midbrain or mesencephalon. Temporal lobe localization is suggested by auditory and gustatory phenomena as aura, and is also suggested by those cases in which there is receptive type of aphasia, the patient in the preheadache phase being unable either to grasp what he hears or to express himself adequately. When the vasomotor disturbance arises in the region of the angular gyrus, the patient has a preheadache aura of a type of spatial disorientation. The migraine-epilepsy relationship has frequently been referred to in literature. Attention has been called to abdominal migraine and abdominal epilepsy. A close relationship has been observed between cyclic vomiting in infancy and periodic headache later in childhood. Urticaria, erythema, pallor, angioneurotic edema, watery nasal discharge, salivation, unilateral hyperhidrosis, and scleral congestion may accompany the migraine attack and imply involvement of the autonomic system.

Western J. Surg., Obst. & Gynecology, Portland, Ore.

60:241-304 (June) 1952

Problem of Prematurity from Point of View of Obstetrician. H. F. Traut.—p. 241.
Prematurity from Standpoint of Pediatrician. W. W. Belford.—p. 249.
Presidential Address: R. E. Fallas.—p. 259.
Experiences with Billroth I Subtotal Gastric Resection. H. G. Moore Jr. and H. N. Harkins.—p. 264.
Acute Pancreatitis: Discussion of Some of Signs and Symptoms. R. E. McKechnie.—p. 276.
Erythroblastosis Fetalis. H. L. Tieche.—p. 280.

West Virginia Medical Journal, Charleston

48:165-218 (July) 1952

Diagnosis of Congenital Heart Disease Amenable to Surgical Therapy. S. Kaplan.—p. 165.
Jaundice. S. Jacobson.—p. 174.
Use of Intra-Arterial Transfusions in Treatment of Myocardial Infarction with Shock. R. O. Bell Jr.—p. 183.
Cancer as Related to Mining Industry in West Virginia. N. H. Dyer.—p. 187.

FOREIGN

Acta Neurologica et Psychiatrica Belgica, Brussels

52:240-310 (No. 5) 1952. **Partial Index**

Medullary Angiomatosis. P. C. Van Reeth.—p. 249.
*Intracerebral Therapeutic Injections that Are Nonmutilating and Non-Necrotizing: Experiences in One Year. P. Abely.—p. 271.
*Treatment of Hemiplegia in Subacute Phase: Organic Hemiplegia Improved by Convulsive Shock. A. Leroy.—p. 281.
New Observations on Schizoparalexia and Schizoparagraphia. J. Bobon.—p. 286.

Intracerebral Therapeutic Injections.—Abely has employed intracerebral injections in treatment of psychoses for about a year in more than 175 bilateral interventions without any surgical accident. The author employs this technique because it produces a minimum of trauma and it is simple and rapid. A blind technique is used because it is easy but effective. In order to avoid mutilation and necrosis, the injection is made at a rather deep point (about 4 cm.) in the middle of the prefrontal centrum ovale, i. e., in a region consisting of fibers and completely free of neurons. In order to effectively infiltrate the prefrontal lobe and to avoid leakage, the injection must be made slowly and usually with successive thrusts, during which the elastic resistance of the brain can be felt. The needle must be held immobile, because the slightest lateral movement may form a draining channel. Isotonic dextrose seemed the ideal vehicle for the drugs to be injected. Manganous chloride of acetylcholine in a stable aqueous solution ("protensyl") was administered in a dose of 1 cc. on each side and seemed particularly helpful in schizophrenic conditions, but *d*-amphetamine tartrate ("maxiton") must be used with great caution, since it is likely to produce severe neurosympathetic reactions. Guyot obtained encouraging results with solutions of placental extracts in patients with involutional psychoses. Tetraethyl ammonium bromide proved effective in five patients with melancholic anxiety who had failed to respond to electroshock treatment. A sixth patient had a fatal vascular collapse. The author feels that anxiety is of cortical origin, and aggressiveness of diencephalic origin. Anxiety disorders are usually favorably influenced by the described intracerebral therapy, but those of the second group usually do not respond or may even be aggravated.

Organic Hemiplegia Improved by Convulsive Shock.—A. Leroy points out that while blockage of the stellate ganglion in cerebral accidents has been used in the treatment of acute disorders of the cerebral circulation, the problem is somewhat different after hemiplegia has existed for some time. In this paper, he describes a woman, aged 58, who had a first stroke in 1948 that resulted in left-sided hemiplegia that gradually subsided. Two years later another stroke again resulted in hemiplegia on the left side, but this time there was progressive exacerbation and mental impairment. One year after the second stroke and three years after the first one, a series of 14 electric shocks was given. A considerable improvement was observed in the organic and mental condition, particularly the hemiplegia. These results confirm the results obtained in two cases previously treated by R. Leroy. The author feels that convulsive therapy may greatly reduce the number of patients with hemiplegia and transform them into active persons. Neither hemiplegia nor hypertension are contraindications to electric shock treatment; on the contrary, thrombotic or embolic causes of hemiplegia are indications for this treatment, particularly when several months have elapsed since the stroke.

British Journal of Dermatology, London

64:213-256 (June) 1952

Seborrhoeic Eczema: Attempt to Define Scope of Term. J. H. T. Davies.—p. 213.
Problem of Pathogenesis of Endogenous Eczema. H. R. Vickers.—p. 225.
Study of New Species of Genus Microsporum. X. Vilanova and M. Casanovas.—p. 231.
Strain of Microsporum Audouini Producing Numerous Macroconidia on Culture. P. J. Hare.—p. 236.

British Journal of Radiology, London

25:281-340 (June) 1952

Radiological Features of Rheumatoid Arthritis. D. E. Fletcher and K. A. Rowley.—p. 282.
*1000 Curie Cobalt Units for Radiation Therapy
I. The Saskatchewan Cobalt 60 Unit. H. E. Johns, L. M. Bates and T. A. Watson.—p. 296.
II. Depth Dose Data and Diaphragm Design for the Saskatchewan 1000 Curie Cobalt Unit. H. E. Johns, E. R. Epp, D. V. Cormack and S. O. Fedoruk.—p. 302.
III. Design of Cobalt 60 Beam Therapy Unit. D. T. Green and R. F. Errington.—p. 309.
IV. Radiation Measurements with Eldorado Cobalt 60 Teletherapy Unit. W. R. Dixon, C. Garrett and A. Morrison.—p. 314.
Placental and Pelvic Angiography by Retrograde Percutaneous Injection of Femoral Artery: Preliminary Report. D. Sutton.—p. 320.
Discussion on Skin Erythema Dose with Röntgen Rays: Some Biological Implications. J. C. Belisario.—p. 326.
Mode of Addition of X-Ray Doses Given with Different Oxygen Concentrations. J. Read.—p. 336.

1,000 Curie Cobalt Units for Radiation Therapy.—Four reports on 1,000 curie cobalt units discuss various aspects of radiation therapy carried out with these units. The use of gamma-emitting isotopes as alternatives to radium therapy is discussed, and it is pointed out that for general radiotherapy radioactive cobalt (Co^{60}) seems particularly suitable. One of the papers describes the 1,000 curie Co^{60} unit that was installed at the University of Saskatchewan in 1951. The activation of the cobalt in the nuclear reactor, the loading of the unit, and the design of the treatment head are described and illustrated. Methods for achieving a low skin dose are discussed, and depth dose data for Co^{60} for a variety of circular fields are presented. Suitable treatment cones have been designed on the basis of experimental work. The design of a Co^{60} beam therapy unit and radiation measurements carried out with these units are described in two other reports.

British Journal of Urology, Edinburgh

24:89-176 (June) 1952. **Partial Index**

*Hyperparathyroidism and Renal Calculi. A. Miller and J. P. Mitchell.—p. 91.
Urinary Aspects of Paraplegia. T. B. S. Dick.—p. 101.
Further Case of Hypernephroma Metastasising to Thyroid. W. E. J. Bennett.—p. 116.
Coexistent Teratoma and Seminoma of Testis. J. K. Mason.—p. 124.
Tumours of Spermatic Cord. H. A. Hashemian.—p. 131.
Fenwick's Ulcer. B. B. Hickey.—p. 134.
Terramycin in Treatment of Infections of Urinary Tract. J. C. Gould, J. G. Macleod and J. D. O'Flynn.—p. 138.
Leiomyoma of Prostate. D. R. Barnes.—p. 152.

Hyperparathyroidism and Renal Calculi.—This paper emphasizes the importance of examining all patients with renal calculi for hyperparathyroidism. The disease may be present even though the stones are unilateral. A review of the literature reveals in all cases the same lengthy history of stones removed at different hospitals until eventually tests are done for overactive parathyroids. A case is described of bilateral renal calculi due to hyperparathyroidism in which no skeletal changes were found. Similar cases reported in the literature are reviewed. The authors believe that the case reported here was diagnosed at an earlier stage than any previously recorded, and it is the only case reported in which there has been no operation for calculi prior to arriving at the diagnosis of hyperparathyroidism.

British Medical Journal, London

1:1207-1260 (June 7) 1952

Allergy and A. C. T. H. G. W. Pickering.—p. 1207.
Accumulation of Diethylaminoethanol Ester of Penicillin in Inflamed Lung Tissue. J. Ungar and P. W. Muggleton.—p. 1211.
Treatment of Hypopituitary Coma. H. L. Sheehan and V. K. Summers.—p. 1214.
Hypopituitarism with Pituitary Tumours: Cortisone in Treatment of Stupor Associated with Hypopituitarism. J. E. Caughey, A. James and E. K. Macleod.—p. 1216.
A. C. T. H. in Hypopituitarism. C. F. Rolland and J. D. Matthews.—p. 1220.
Tubo-Uterine Implantation. V. B. Green-Armytage.—p. 1222.
Sulphone and Streptomycin in Pulmonary Tuberculosis. P. W. Edwards, A. C. Penman and L. J. Cutbill.—p. 1224.
Megaloblastic Anaemia of Infancy. A. G. Rickards.—p. 1226.
Tuberculosis in Mental Hospitals. B. T. Mann.—p. 1228.

Deutsche medizinische Wochenschrift, Stuttgart

77:733-764 (June 6) 1952. **Partial Index**

Reflex and Painful Symptoms of Cardiac Diseases. G. Damm.—p. 734.
Migraine as Symptom of Reduced Cerebrospinal Fluid Pressure. H. von der Burchard.—p. 736.
Significance of Focal Dental Infection in Obstetrics and Gynecology. H. Gänssbauer.—p. 738.
Report on Epidemic of Virus Meningitis. H. Assmann.—p. 740.
*Results of Treatment of Subacute Bacterial Endocarditis with Penicillin and Streptomycin. E. Fritze and E. Nasse.—p. 745.

Penicillin and Streptomycin in Subacute Bacterial Endocarditis.—Of 140 patients with subacute bacterial endocarditis treated at the medical clinic of the University of Göttingen between 1946 and 1950, 113 received antibiotic therapy. Of the 113 patients 63 (56%) died of endocarditis or cardiac decompensation. In five patients necropsy showed that the endocarditis had been cured and that death resulted from cardiac decompensation or from other causes. Of the remaining 50 patients, 22 recovered, 24 were definitely improved, and in 4 improvement was doubtful. Of the 27 patients who were not given antibiotic treatment because their condition was considered hopeless, 25 died. Of the 113 patients treated with antibiotics 78 were given 500,000 to 1,000,000 units of penicillin daily for four to six weeks; of these 78 patients, 13 were cured, 9 who had been followed up for more than one year were considerably improved, and 56 died. Of the remaining 35 patients who were given 2,000,000 to 10,000,000 units of penicillin daily for two to four weeks and partly combined with 1 to 3 gm. of streptomycin daily, 9 were cured, 19 who had been followed for less than one year were considered as temporarily cured, and 7 died. While a recovery rate of only about 20% was obtained with smaller doses of penicillin administered for four to six weeks, the recovery rate was increased to about 80% with large doses of penicillin, particularly if they were combined with streptomycin therapy. In general a cure may be obtained with daily doses of 1,000,000 to 2,000,000 units of penicillin for four to six weeks in cases of subacute bacterial endocarditis due to Streptococcus viridans, while large doses up to 10,000,000 units of penicillin and occasionally combined with 1 to 3 gm. of streptomycin daily for two to four weeks may be required in cases of subacute bacterial endocarditis due to enterococci and other bacteria less susceptible to penicillin and in cases with apparently negative bacterial culture.

Gazzetta Medica Italiana, Milan

111:71-101 (March) 1952. **Partial Index**

*Treatment of Some Transfusion Reactions with Histamine-Antagonizing Agent. P. L. Alfonsi.—p. 71.
Lactogenic Action of Antistine. V. Rindi.—p. 73.

Antazoline in Blood Transfusion.—Antazoline (antistine®) was added in the proportion of 200 mg. for 500 cc. of blood in 350 of 738 transfusions at the surgical clinic of the University of Florence. Blood without antazoline was given to 350 patients, who served as controls, and 38 received blood that probably contained proteins since the donors had not been fasting. Antazoline was used because it is one of the most effective antihistamine agents, is better tolerated locally, and is less toxic. Febrile reactions with chills were observed in 53 (15%) of the control patients and in 14 (4%) of the others. Intravenous injection of 200 mg. of antazoline in 10 cc. of distilled water had no effects on these reactions, which subsided in 15 to 20 minutes as they usually do. There were 12 instances of urticaria and 3 of wheal-like eruption in the control group, while no allergic reaction was seen in the others. The eruption, itching, and feeling of heat disappeared with intramuscular injection of 200 mg. of antazoline. Only two of the 38 patients who received blood of nonfasting donors to which antazoline had been added had febrile reactions. Thus, antazoline decreased the number of transfusion reactions. The author attributes the febrile reactions in persons who received blood with antazoline to the presence of nonprotein pyrogens that do not have antigen properties.

J. Franç. Méd. et Chir. Thorac., Paris

6:201-296 (No. 3) 1952

*Bronchial Infection in Asthma. R. Kourilsky, G. Decroix, M. Blondeau and Y. Ganter.—p. 201.
*Aspergilloma Causing Bronchiectasis. O. Monod, G. D. Pesle and M. Labeguerie.—p. 229.
Diaphragmatic Hernia (Partial Agenesis of Half of Left Diaphragm): Plastic Repair of Diaphragm with Atelectasic Lung. M. Bonilla-Naar, A. M. Corredor and Savogal.—p. 244.

Bronchial Infection in Asthma.—The authors demonstrated that in many cases the onset of asthma is caused by an infection of the submucosa and that chronic asthma with expectoration is always due to superimposed infection. Only 10 of 28 patients with asthma had normal sinuses. Infection of the upper respiratory tract was latent purulent maxillary, frontal or ethmoidal sinusitis, or chronic purulent rhinitis. Comparative studies of the bacterial flora of the sputum, nasopharynx culture, and expectoration revealed the presence of infection, especially in patients in whom expectoration was copious. Bronchoscopy revealed that the mucous membranes of the bronchi were red, congested, and dark. Bronchial biopsy revealed inflammation of the bronchi that was not detected clinically or bronchoscopically. The infection preceded asthma in 20 patients, and was concurrent in 3, secondary in 4, and asbent in 1. The role of infection as a main cause of asthma becomes more important as the patient grows old, and the search for the source of infection should be the principal aim in middle-aged persons in whom asthma seems to occur without a warning factor. Some of the authors' patients had an infection of the gums and teeth, while in others the attacks were preceded by mild infection of the rhinopharynx, especially at the beginning of a new season. In chronic asthma bronchial infection seems to play the role of a local factor of reactivation. The failure of antibiotic therapy can be easily understood, since infection is not the only cause of spasm, and treatment must also be directed toward the nutritional and psychic factors involved.

Aspergilloma Causing Bronchiectasis.—Aspergilloma designates a form of pulmonary mycosis limited to a single lesion caused by an Aspergillus organism in a dilated bronchus in which bronchiectasis is secondary to this lesion. Symptoms leading to a correct diagnosis are repeated hemoptysis, absence of Myco. tuberculosis, and sometimes presence of mycelium in the expectoration. The roentgenogram is characterized by an area of uniform opacity surrounded by a clear area. Its size remains unchanged. The lung tissue remains normal, and there is never atelectasis because of pulmonary obstruction. Identification of fungi is the best diagnostic means, but the skin reaction to Aspergillus, angiography, and bronchoscopy are also helpful. Parafinoma, cholesterol tumors in the lungs, hydatid cysts, and tuberculoma should be differentiated on roentgenograms. Radium, iodine, and antibiotic therapy as well as injection of iodized oil (lipiodol® [40% iodine]) into the bronchi is unsuccessful. Segmentary resection is the treatment of choice. Three cases are described.

Medical Journal of Australia, Sydney

1:593-624 (May 3) 1952

Gastritis: Study of 112 Cases Diagnosed by Gastric Biopsy. R. K. Doig and I. J. Wood.—p. 593.
Correlation Between Test Meal Findings and Histology of Stomach as Shown by Gastric Biopsy. J. F. Funder and S. Weiden.—p. 600.
Gastric and Duodenal Ulcer: Survey of 141 Cases. R. K. Doig and I. J. Wood.—p. 602.
Some Radiological Aspects of Tuberculous Disease of Bones and Joints. B. E. Frecker.—p. 606.

1:625-656 (May 10) 1952

Chemotherapeutic Advances in Tropical Diseases of Importance to Australia. N. H. Fairley.—p. 625.
Enumeration of Eosinophile Cells: Analysis of Errors Involved. S. Wiener.—p. 633.
Correction of Nasal Deformities. F. Shanasy.—p. 635.
Effect of Para-Aminosalicylic Acid on Allergic Process. E. R. Trethewie.—p. 638.

Minerva Medica, Turin

43:701-728 (April 5) 1952

"Three-Branched" Clamp for Side-to-Side Anastomosis of Aorta and Pulmonary Artery. A. M. Dogliotti and G. Guglielmini.—p. 701.
*Retroperitoneal Insufflation in Roentgenographic Investigation: Technique and Results. G. Sansone.—p. 705.

Retroperitoneal Insufflation in Roentgenographic Diagnosis.—Ruiz Rivas' retroperitoneal insufflation with oxygen to explore the abdominal organs of children is easy to perform, innocuous, and inexpensive. With the child in knee-chest position the needle is introduced at the level of the sacrococcygeal point, 1 or 2 cm. beyond the inferior border of the sacrum. It is inserted obliquely upward, inward, and forward so that the point lies in the presacral cellular tissue or in the retrorectal space as near as possible to the anterior surface of the sacrum and in its midline. Once the gaseous space is obtained in the pararectum, the oxygen continues to advance following the paths of least resistance pressing from the abdomen to the thorax through the various openings in the diaphragm. Sometimes, especially in thin patients, emphysema of the neck is produced. With this method outlines of organs, such as the psoas muscles, kidneys, liver and spleen, and sometimes bladder and colon, are obtained. The outline of the pancreas, however, does not appear, perhaps because certain anatomic reasons prevent peripancreatic infiltration. The author prefers to perform the puncture with the child lying on one side and inserting the needle toward the ventral surface of the coccygeous on the anococcygeal line. He uses large 100 or 200 cc. syringes and the dose of oxygen ranges from 200 or 300 cc. for infants to 1,000 cc. for 11 and 12-year-old children. Radiographs are taken 10 minutes after the injection, and no inconveniences are observed. This method is particularly indicated for roentgenograms of the kidney. Radiographs are much better when retroperitoneal insufflation is combined with endovenous or retrograde pyelography, or body section roentgenography in the frontal, sagittal or axial transversal positions. This method combined with body section roentgenography in the axial transversal position is particularly indicated in cases of tumor of the kidney, as shown by the author's two years' experience with 12 patients. He also used retroperitoneal insufflation in one patient with a tumor of the adrenal and bone metastasis, one with abdominal lymphosarcoma, and one with a mesenteric cyst. In the last patient previous urography and roentgenography with barium failed to show the presence of the mass.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

96:1245-1312 (May 24) 1952. **Partial Index**

Multiple Exsanguinations in Treatment of Kernicterus. G. M. H. Veeneklaas.—p. 1246.
Food Poisoning Caused by Salmonella Bovis Morbificans. A. Pieron, A. Clarenburg and H. Beeuwkes.—p. 1251.
*Brill-Symmers Disease a Reticulosis. H. E. Schornagel.—p. 1254.
Congenital Stridor Caused by Congenital Laryngeal Cyst. A. C. Nieuwenhuijse and A. van Lookeren Campagne.—p. 1262.

Brill-Symmers Disease a Reticulosis.—Schornagel points out that several cases of a disease identified as "generalized giant follicle hyperplasia of the lymph nodes and spleen" were reported in 1925 by Brill, Baehr and Rosenthal, who found that roentgen therapy restored these patients to health but did not necessarily cure them. Later, when the malignant character of the disease was recognized, it was designated as malignant follicular hyperplasia, and since the morphological aspects of the disease were chiefly investigated by Brill and Symmers, it became known as Brill-Symmers disease. Schornagel describes observations he made in autopsy studies on three patients with Brill-Symmers disease, and says that in an additional six cases the diagnosis of Brill-Symmers disease was made on the basis of biopsy material. The ultimate prognosis is not favorable in this disease, but patients may remain in a fairly favorable condition for as long as 15 or 20 years. The author regards this form of reticulosis as presarcoma.

Nordisk Medicin, Stockholm

47:613-652 (May 9) 1952. **Partial Index**

Homotransplantation of Arterial Segments Stored in Blood Vessel Bank: Preliminary Report on Experimental Studies in Dogs. T. Hiertonn.—p. 617.
*Cultures from Laryngeal Swabs for Quantitative Evaluation of Bacilli Discharge in Tuberculosis: Significance in Practical Tuberculosis Work. K. Smedsrud.—p. 623.
Skin Permeability in Pregnancy. L. Ploman.—p. 626.
Blood Transfusion in Bleeding Peptic Ulcer. E. Jespersen and O. C. Olsen.—p. 628.
Hematopericardium Following Blunt Trauma Against Thorax. S. Benestad.—p. 630.
Risk in Using Bougies for Dilatation of Deep Bile Ducts. A. Langvad-Nielsen.—p. 632.

Cultures from Laryngeal Swabs in Tuberculosis.—To test the relative sensitivity of cultures from sputum and laryngeal swabs in patients known to be discharging tubercle bacilli, 71 simultaneous double cultures were made from expectorate and larynx in 17 patients. Fourteen double cultures were negative. Of the remaining cultures 55 from the sputum and 36 from the laryngeal swabs were positive. In the six patients with distinct, and often large, cavities the sputum cultures were positive in all of the 33 double cultures, and the laryngeal cultures in 32 cases. In the 11 patients with doubtful cavities and doubtful destructive processes 24 double cultures gave 20 positive sputum cultures and 2 positive cultures from laryngeal swabs. Smedsrud thus finds that positive cultures from laryngeal swabs mean abundant discharge of bacilli, and negative cultures mean few bacilli or no bacilli discharge. Positive laryngeal swabs testify for collapse treatment, due attention being paid to the roentgen picture and the results of bronchoscopy and to the clinical character and tendency of the process. Unless the roentgenogram in itself strongly indicates collapse treatment, expectant treatment is suggested when the laryngeal swabs are negative.

Presse Médicale, Paris

60:881-900 (June 14) 1952

*Effect of Hydrazine of Isonicotinic Acid in Treatment of Renal Tuberculosis. R. Couvelaire, J.-R. Debray and A. Desmonts-Cros-Decam.—p. 881.
*Fatal Accidents Following Sternal Puncture. J. Oimer and G. Knebelmann.—p. 882.
Thirty-Four Cases of Cirrhosis Followed-Up in 1951. P. Uhry and A. Morel-Maroger.—p. 883.

Isonicotinic Acid Hydrazide in Renal Tuberculosis.—Isonicotinic acid hydrazide was given for three weeks to one month to nine patients with renal tuberculosis in doses of 250 mg. daily, with 100 mg. given in the morning and evening and 50 mg. at noon. Pus and Mycobacterium tuberculosis persisted in the urine of all the patients; the bacilli maintained their normal characteristics and their number did not change. Streptomycin, *p*-aminosalicylic acid, and amithiozone were then substituted for or combined with the hydrazine of isonicotinic acid in the treatment of the nine patients, four of whom are reported on in detail. Within three days the tubercle bacilli disappeared from the urine of one patient, who had been given streptomycin, *p*-aminosalicylic acid, and amithiozone without the hydrazine of isonicotinic acid, and from the urine of another patient, who was given streptomycin and *p*-aminosalicylic acid combined with the hydrazine of isonicotinic acid. It thus was demonstrated that these two cases were not refractory to conservative treatment. In the two other cases the tubercle bacilli persisted in the urine despite treatment with streptomycin and *p*-aminosalicylic acid without and in combination with the hydrazine of isonicotinic acid. Nephrectomy was performed, and the presence of cavities in the inferior and superior pole suggested that surgical treatment may be indispensable in cases in which the tubercle bacilli in the urine are refractory to chemotherapy.

Fatal Sterna' Puncture.—As a rule sternal puncture can be considered a safe procedure. Two cases of death following sternal puncture in a 17-year-old girl and a 13-year-old boy with febrile splenomegaly are reported by the French authors. The symptomatology of the fatal accident in these cases corresponded with that in the cases reported in the literature. There was an initial

syncope, followed by temporary improvement and then by cyanosis and cerebral anoxia, with ensuing death. Results of necropsy suggested that the mechanism of death seems to be closely connected with a perforation of the internal table of the sternum, entailing a laceration in the myocardium associated with intrapericardial hemorrhage. Cases of death following sternal puncture are rare and do not contraindicate sternal marrow aspiration, but suggest that the performance of the puncture requires increased precaution in gently withdrawing the needle if on aspiration no fluid is obtained in the syringe, and by strict avoidance of the exertion of force.

Revista Paulista de Medicina, São Paulo

40:247-306 (April) 1952. **Partial Index**

*Thrombo-Angiitis Obliterans and Arteriosclerosis Obliterans. L. E. Puech Leão and J. Bueno Neto.—p. 247.
Segmentary Resections in Treatment of Pulmonary Tuberculosis. E. de J. Zerbini.—p. 257.
Results of Repeated Weekly Doses of Oral BCG in a Case of Fixed Lupus Erythematosus. L. Baptista and N. Belliboni.—p. 265.

Thromboangiitis Obliterans and Arteriosclerosis Obliterans.—Specific methods of treating obliterative peripheral vascular disease are hard to evaluate because a part of the improvement secured results from general therapeutic measures such as rest, prohibition of smoking, and local hygiene, which often vary from one patient to another. This difficulty was eliminated in a group of 104 patients with chronic peripheral vascular disease treated by a number of specific methods, because they all received the same general care. The patients were classified in four groups according to the severity of the disease: group 1 had ischemia on effort (intermittent claudication); group 2 had ischemia (pain) while at rest; group 3 had ulceration or gangrene in small distal areas; and group 4 had extensive gangrene. Results of treatment were considered good if the affected limb was saved and cicatrization of lesions occurred, even though minor amputations were required. The results were considered bad if the limb was lost or the disease progressed to such an extent that it passed into the next more advanced group. These criteria are admittedly crude, but were adopted because of their simplicity and because there is at present no known cure for the conditions. Treatment (excluding group 4 cases requiring amputation) consisted of administration of carbogen (a mixture of oxygen and carbon dioxide) alone, carbogen in combination with other agents, hypertonic sodium chloride, sympathectomy, and a few miscellaneous medications such as procaine (novocaine®) and hormones. Analysis showed that thromboangiitis responded to treatment better than arteriosclerosis, regardless of the method used. The best results were obtained with sympathectomy (70.8% of 24 interventions); hypertonic sodium chloride injections were the least effective treatment. A pessimistic attitude in the presence of small areas of ulceration or gangrene was not found to be justified; the majority of the patients with such lesions were able to retain useful limbs, in spite of minor amputations, when appropriate treatment was given. The duration of the disease apparently has a greater influence on the outcome than the extent of the arterial obstruction; early diagnosis improves the patient's chances for successful palliative treatment.

Riforma Medica, Naples

66:505-532 (May 10) 1952. **Partial Index**

*Surprising and Quick Therapeutic Action of Isonicotinic Acid Hydrazide in Severe Tuberculous Infections of Mouth, Pharynx and Larynx. N. Sanguigno.—p. 505.
Findings of Target Erythrocytes in Blood Conditions Other Than Cooley's Anemia. C. Piovella.—p. 507.
Ancylostomiasis in Puglia Region: Preliminary Report. N. Mongelli-Sciannameo.—p. 510.

Isonicotinic Acid Hydrazide in Local Tuberculous Lesions.—The effects of isonicotinic acid hydrazide on severe tuberculous lesions of the tongue, palate, and upper respiratory tract are reported. A 29-year-old man who had had pulmonary tuberculosis for 10 years was admitted with infiltrating ulcerous laryngitis involving the pharynx, palate, and tongue. His general condition was extremely poor; speech and swallowing of saliva and fluids were difficult. The right side of the soft palate, the uvula, and the right tonsil had superficial grayish ulcerations; a yellow, thick, and granulous exudate covered the posterior surface of the tongue and extended to its sides. Smears of this exudate revealed numerous Myco. tuberculosis. Treatment with streptomycin, *p*-aminosalicylic acid, and thiosemicarbazone failed. Administration of one 100 mg. tablet of isonicotinic acid hydrazide ("nicotibina") for two days caused greater elevation of temperature. With two 100 mg. tablets daily temperature returned to normal, and the ulceration of the tongue, palate, and pharynx began to heal. After 20 days the patient was improved and able to eat food. Two months later he was still receiving the drug, but had not had fever for 45 days and had gained 6 kg. Bacteria, which were numerous at the beginning of therapy, had disappeared, and a culture 40 days later was still negative. The erythrocyte sedimentation rate decreased gradually. Improvement of the clinical and radiological picture of the thorax was only mild. Isonicotinic acid hydrazide was given also to a 42-year-old man with chronic bilateral pulmonary tuberculosis, severe cardiorespiratory insufficiency, and large tuberculous ulcerations of the tongue. The patient survived for 31 days, during which the ulceration of the tongue, which had not responded to previous antibiotic treatment, healed completely.

Wiener medizinische Wochenschrift, Vienna

102:483-530 (June 28) 1952. **Partial Index**

Hypophysial Disturbances in Psychoneuroses. L. Beichl.—p. 485.
*Use of Norepinephrine (Arterenol) During and After Operations. H. Bergmann.—p. 488.
Question of Postoperative Circulatory Disturbances. H. Fegerl.—p. 492.
Surgical Treatment of Female Sterility. G. Halter.—p. 495.
Infectious Mononucleosis. W. Herbinger.—p. 500.
Value of Prostigmin Test in Diagnosis of Pancreatic Disorders. W. Lutz.—p. 509.
Goiter as Deficiency Disease. M. Richard.—p. 511.
*Sympathectomy and Sexual Function. F. Rosenauer.—p. 519.

Use of Arterenol (Norepinephrine) During and After Operations.—After briefly reviewing the physiological and pharmacological effects of arterenol, Bergmann summarizes previous clinical reports and then describes his own experiences with arterenol during and after surgical operations. He employed arterenol in 32 patients for postoperative surgical collapse and in 34 cases to counteract hypotension in simple or continued spinal anesthesia. If duration and dosage of arterenol administration is adapted to the individual case and circumstances, results can be obtained that surpass those of any other circulatory stimulant. The most effective mode of administering arterenol to surgical patients is by intravenous drip infusion. The patient must be kept under constant observation; the blood pressure must be observed at short intervals and the rapidity of infusion must be adjusted to the blood pressure values. Considerably higher doses than those indicated in literature reports are tolerated and are effective. However, prolonged infusion of highly concentrated solutions may produce necrosis in the region of the vein used for infusion. This occurred in two of the three cases that are reported in detail.

Sympathectomy and Sexual Function.—Rosenauer reviews literature reports and describes his own observation on changes in the sexual functions of man following sympathectomy. While there have been patients, including some operated on by Rosenauer, in whom sexual impotence improved after lumbar sympathectomy, impotence has also been known to result from sympathectomy. Rosenauer found that impotence resulted in two cases in which the first lumbar ganglion had been removed on both sides. Literature reports as well as his own observations suggest that an important peripheral sympathetic nerve center for sexual potency is located in the upper lumbar truncus sympathicus. For this reason he regards it as advisable to preserve at least the uppermost lumbar ganglion in case of bilateral lumbar sympathectomy. He suggests that in the surgical treatment of hypertension, the extensive Smithwick operation be replaced by combined thoracolumbar sympathectomy, to be carried out in several stages. The uppermost ganglion of the lumbar sympathetic trunk should be preserved. Removal of sacral ganglions to improve the impaired circulation of the lower extremities is regarded as inadvisable by the author, because it produces only slight improvement in circulation and yet involves the danger of disturbances in sexual potency.

BOOK REVIEWS

Normal Blood Pressure and Hypertension: New Definitions. By Arthur M. Master, M.D., Cardiologist, Mount Sinai Hospital, New York, Charles I. Garfield, M.D., Research Assistant in Cardiology, Mount Sinai Hospital, and Max B. Walters, M.D., F.R.C.P. Cloth. $4. Pp. 144, with 36 illustrations. Lea & Febiger, 600 S. Washington Sq., Philadelphia 6, 1952.

The authors of this excellent monograph are well qualified to deal with the problem of the limits of normal blood pressure. It is a vexing and important issue, the more important because physicians often fail to recognize that a measurement of blood pressure that seems abnormally high is not equivalent to a diagnosis of essential hypertension. As a result, many persons live out a normal life span and die of extravascular causes, beset by the doubts, fears, and social and economic inconveniences created by the too hasty diagnosis of "high blood pressure."

What it comes to is that the authors show that the present day upper limits of "normal" have been arbitrarily set too low. Some physicians will recall that the view was promulgated some years ago that the upper limit of normal should be 120/80 mm. Hg. At that time, common sense indicated that this opinion was in error. Now, at last, data have been objectively and carefully collected that validate this impression and that also demonstrate the influences of weight, sex, and age on arterial pressure. The conclusions correspond well with clinical experience.

From a technical standpoint the book is good, with excellent illustrations and an adequate bibliography. There is also an interesting, well-written section on the history of sphygmomanometry. The book is recommended without reservation.

Medical Group Practice in California. By E. Richard Weinerman, M.D., and George S. Goldstein. Paper. Pp. 28. School of Public Health, University of California, Berkeley 4, 1952.

This pamphlet is a study of group practice in California in 1950 as it compares with the 368 medical groups in the United States as a whole studied by Hunt and Goldstein in 1946. The authors defined a "true general medical group" as follows: "1. A systematic association of at least three full-time physicians; 2. More than one specialty of medicine represented; 3. Joint use of office facilities and auxiliary personnel; 4. Formal organization for administration and financing; 5. Pooling of income and sharing of common overhead expenses with net payments to physicians made according to a pre-arranged plan." This is similar to the Hunt and Goldstein definition and differs only slightly from that used by the Bureau of Medical Economic Research of the American Medical Association.

The authors have done a thorough job on statistical data. They determined that 52 groups definitely satisfied their definition out of an original list of 123; 29 groups did not respond. Data on the 52 groups were tabulated on such varied subjects as age and size of group in relation to community size, distribution of groups and physicians in groups with and without prepayment plans, criteria of remuneration to physicians, and benefits for physicians.

In general, the book gives a good and reasonably complete statistical picture of the groups studied. Its major weakness lies in one of the conclusions stated in the summary. "The potential of group medical practice is most fully expressed when office and hospital facilities are coordinated and when group health services are prepaid." This statement is definitely controversial, and its place in this study is questionable, since no data are developed on the quality of medical service provided by the clinics of either the prepayment or the fee for service types of organization. Beyond this, although the data are biased by the presence of four extremely large groups, the information is, for the most part, objective and useful. The authors point out the influence of the large organizations on the study and the differences in the data that occur when they are excluded.

The reviews here published have been prepared by competent authorities and do not represent the opinions of any official bodies unless specifically stated.

Patterns of Organization in the Central Nervous System: Proceedings of The Association, December 15 and 16, 1950, New York, N. Y. Research Publications, Association for Research in Nervous and Mental Diseases, Volume XXX. Editor: Philip Bard, Ph.D. Cloth. $12. Pp. 581, with 268 illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1952.

The 25 papers that make up this volume are all by different authors and summarize the results of laboratory investigations. The papers are grouped into four sections. The first consists of seven papers dealing mainly with peripheral nerves and spinal reflexes, the second (five papers) with motor nerves and cortical motor areas, the third (four papers) with the cerebellum and brain stem, and the fourth (nine papers) with sensory phenomena and integrations at higher levels. Each section concludes with a résumé in which an authority brings out the most significant points in the preceding papers.

This device, together with the fact that the papers are extremely well written, goes far toward making the book interesting to the general medical reader. It will probably be some time before all the ideas expressed are fully appreciated and find their ultimate clinical application. An instance is the work reported in the first chapter on the curious process whereby the nerves in transplanted limbs in urodeles establish their connection with the central nervous system. The resulting persistent, useless, or hindering movements of these limbs suggest that this work must have important bearing on the problems of cerebral palsy, chorea, obsession, and compulsion. A hopeful sign of progress here is the interesting convergence of the vocabulary of the neurophysiologist with that of the electronic engineer. While the authors of this book think much in terms of resonance, tuning in, modulation, and feedback, the recent literature of the electronic engineer abounds in terms like memorize, scan, forget, recite, and double-recite. The experimental techniques described in this book also illustrate this point, for they abound in amazing applications of electronic science, just as the excellent series of technical monographs from the Bell Telephone Laboratories, Inc., abound in applications of physiology and psychology in the field of communication. Progress in both areas is such as to justify high hopes for an early solution to many problems of human health and conduct.

Readers who have had the experience of concentrating on a long and difficult volume only to find themselves harvesting a crop of ill-considered and inaccurately expressed ideas are inclined to be wary of attacking something as formidable as this book. In the present instance, however, they can be assured that it is written with extraordinary care and that the effort of reading is well rewarded. There are many useful references and a good index. The physical makeup is not only attractive but also helpful.

The Apologie and Treatise of Ambroise Paré Containing the Voyages Made into Divers Places with Many of His Writings upon Surgery. Edited and with introduction by Geoffrey Keynes, M.D., F.R.C.S., F.R.C.O.G. Cloth. $3.50. Pp. 227, with illustrations. University of Chicago Press, 58th St. and Ellis Ave., Chicago 37, 1952.

This is a reprint from texts brought out in Canada and England that are covered by international copyright, but it is none the less a welcome addition to the literature concerning one of the greatest surgeons of all time. Paré had a full measure of wisdom; his observations were acute, and his reasoning was correct. His skill in recording all essential details commands respect.

Born in 1510, he came to know the horrors of war; this gave him the opportunity to satisfy his great curiosity as to the human body and its power to resist death from the wounds of conflict. In those days, one succeeded if he could attach himself to the noble or great. Paré's father was valet and barber to Sieur de Laval and probably did whatever surgery came his way. In this, he was observed by his gifted son, Ambroise. There was a faculty and surgeons' college, the members of which were at odds with the barber-surgeons; therefore, Ambroise ran into

conflicts with the learned gentlemen. Like Shakespeare he is said to have had "little Latin and less Greek," but one wonders how he became so well acquainted with the writings of Hippocrates, Galen, and the other founding fathers of surgery. His first "job" seems to have been with the monastic Hôtel-Dieu, the only public hospital in Paris at that time, but he left it to "join up" with Mareschal de Montejan of the French infantry. He soon began to experiment with boiling oil in the treatment of war wounds. He soon gave this up and began to work with ligatures instead of caustics in controlling hemorrhage. Strangely enough, tying off vessels incurred great opposition, but Paré's written reply in favor of his method is a masterpiece of logic supported by many extracts from the literature. The "voyages" made to diverse places, Turin, Perpignan, Metz, Hedin, Moncontour, St. Denis, and Bayonne, seem to have been journeys in search of further surgical experiences.

His surgical writings deal with operative procedures in aneurysms, hernia, amputations, fractures, dislocations, management of gunshot wounds, and even cataracts of the eye. The chapter on fractures makes interesting reading today because our methods of examination, except x-ray, are based on keen special sense organ development, use of eye, ear, and hand, and deductions from observations gleaned through experience.

Finally, Paré teaches his confreres how to make reports of wounds and deaths to those in authority, so that the law may be properly served and the wicked be made to suffer for their sins against society. All this is fascinating, chiefly because it is a study of the human mind at work to relieve disease and suffering and to prevent death when possible. To rationalize concerning the keen intellect of Paré is to realize once more that "there were giants in those days."

Cerebral Palsy Institute Proceedings, November 1950. Prepared by Marguerite Abbott, B.S., O.T.R., Executive Director, Coordinating Council for Cerebral Palsy in New York City, Inc. Sponsored by Coordinating Council for Cerebral Palsy in New York City, Inc. Paper. $1.50. Pp. 136. Association for Aid of Crippled Children, Inc., 580 Fifth Ave., New York, N. Y., [n.d.].

This manual is a compilation of talks on cerebral palsy that were given before a group of physicians and lay therapists. There is much useful information in this book, particularly on some of the medical aspects of cerebral palsy and on speech and occupational therapy; however, the usual fault of most such compilations is present, in that there is no unity of viewpoint or homogeneity in quality of contexts. Thus, in part of the discussion on the organizational aspects of the cerebral palsy problem, there are one or two page abstracts of what was apparently a good exposition by an able lecturer but which in abbreviated form does not give the reader much information.

This manual might be useful as a basis for setting up a graduate course in cerebral palsy but would not be too valuable for source material in all the aspects that the titles purport to cover. Nevertheless it would be of value to occupational therapists and physical therapists and other lay therapists who were seeking a broad view of the subject. In addition, several of the papers on the medical aspects of cerebral palsy would have informational value to interested physicians.

Bone Tumors. By Louis Lichtenstein, M.D., Senior Pathologist, General Medical and Surgical Hospital, Veterans Administration Center, Los Angeles. Cloth. $10.50. Pp. 315, with 155 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1952.

The introductory chapter of this text emphasizes that shadows in roentgenograms afford no fixed formula for clinical diagnosis but must be correlated with tissue examination before any treatment of a suspected bone tumor is attempted. The author classifies tumors of the bone as derivatives of (1) cartilage cells or cartilage forming connective tissues, (2) osteoblastic connective tissues, (3) nonosteoblastic connective tissues, (4) mesenchymal connective tissues (Ewing's tumor), (5) hematopoietic tissues, (6) nerve tissues, (7) vascular tissues, (8) fat cells, (9) notochordal tissues, and (10) adamantine tissues. The chapters on the bone tumors describe the clinical features, pathology, radiograms, therapy, and prognosis of (1) osteochondroma, (2) solitary enchondroma, (3) benign chondroblastoma, (4) chondromyxoid fibroma, (5) osteoid osteoma, (6) osteogenic fibroma, (7) nonosteogenic fibroma, (8) giant cell tumor, (9) vascular tumors, (10) nerve tumors, (11) chondrosarcoma, (12) osteogenic sarcoma, (13) fibrosarcoma, (14) Ewing's tumor, (15) multiple myeloma, (16) hematopoietic tissue tumors, (17) liposarcoma, (18) chordoma, (19) adamantinoma, and (20) metastatic carcinoma. In the appendix, some lesions of bones mistaken for tumors are discussed.

The text is illustrated by numerous radiograms of good quality, photographs of the tumors, and photomicrographs of tumor tissues. The descriptive material is adequate. Surgeons and pathologists will find this book useful.

Urine and the Urinary Sediment: A Practical Manual and Atlas. By Richard W. Lippman, B.S., M.D., Research Associate, Institute for Medical Research, Cedars of Lebanon Hospital, Los Angeles. Cloth. $7.50. Pp. 124, with 61 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, 1952.

The purpose of this monograph is to serve as a guide to clinicians for the examination of urine and urinary sediment and to correlate the findings with disease. The book is divided into three chapters. The newer concepts of proteinuria and its significance and consequences are discussed in chapter 1. There is a concise discussion of all the elements of urinary sediment with 36 excellent color photographs illustrating these elements as they appear under the microscope. Chapter 2 correlates the renal lesions found in various diseases with what is found in the urine. These diseases are grouped under the following headings: development anomalies, obstruction of the urinary tract, vascular diseases, bacterial infection, renal manifestations of neoplasia, diseases of hypersensitivity, metabolic diseases, and toxic agents. There are 20 color photographs showing microscopic sediments typical of various diseases. Techniques for all the routine tests on urine that are helpful in diagnosis are discussed in chapter 3. A number of special tests are included, among which are the Addis count, quantitative protein and chloride, the Mosenthal concentration test, and a stain for malignant cells.

The book is written in a readable style. It is well organized and printed, with 56 beautiful colored microphotographs. There are 93 up-to-date references. This monograph should appeal to clinicians, clinical pathologists, and technicians.

Lehrbuch der Kinderheilkunde. Begründet von Prof. Dr. Emil Feer. Herausgegeben von Prof. Dr. Hans Kleinschmidt. Seventeenth edition, by Prof. Dr. J. Ibrahim, et al. Cloth. 32 marks. Pp. 790, with 274 illustrations. Gustav Fischer, Villengang 2, Jena 15, 1952.

This excellent pediatric textbook, originally created by Dr. Feer, continues to preserve the high standard and reputation that it has enjoyed for many years.

The text is readable, and each chapter is prepared with much sound thinking and mature judgment. The book is arranged according to the well-known principles of a classic, standard pediatric textbook. At the end is an 18 page table of drugs that are useful in pediatric practice, with indications for their use and proper dosage. This is a helpful feature, which is rarely found in American texts.

The illustrations are well chosen and of good quality. The only adverse criticism one might offer concerns the binding of the book. Although printed on good paper, a feature not always found in European textbooks, the binding is poor and, one is afraid, won't withstand much handling.

This book conforms more closely to American pediatric thinking than any other pediatric text recently published in Europe. It is highly recommended.

A Course in College Chemistry. By V. R. Damerell. Cloth. $5.50. Pp. 587, with illustrations. The Macmillan Company, 60 Fifth Ave., New York 11, N. Y., 1952.

This copiously illustrated text is for students who do not intend to become chemists. Consequently, the topics usually emphasized in the first course in college chemistry are treated briefly, and stress is laid on the application of chemistry, inorganic, organic, and physical, in ordinary living. The quality of the writing and of the printing and binding justifies the cost of the book.

QUERIES AND MINOR NOTES

SEVERE COUGH FOLLOWING COMMON COLDS

TO THE EDITOR:—*Is there good reason for withholding antibiotics in the treatment of such conditions as sinusitis, otitis, pharyngitis, and tracheitis, with no fever, secondary to a common cold? In addition to the danger of sensitivity to the drug developing and the possibility of the bacteria of the upper respiratory tract becoming resistant to the antibiotics, is there evidence that such treatment may prevent the development of immunity to these organisms so that the disease returns more easily? What treatment is advisable for the prophylaxis and relief of an otherwise healthy person who has a severe cough for a long time after each common cold?* *M.D., Tennessee.*

ANSWER.—A hard and fast rule cannot be established for either using or withholding antibiotics in fever-free complications of the common cold. Much depends on the clinical course of these disease entities, the physician's familiarity with previous upper respiratory tract disease episodes of the individual patient, and the response of the patient treated to a regimen of conservative therapy as well as to chemotherapy or antibiotics. There is no evidence that the use of antibiotics in acute upper respiratory tract infections prevents the development of immunity so that respiratory disease returns more readily.

Since there is no effective prophylaxis of the common cold, the same is equally true of the common cough; however, a number of general measures are useful in cough therapy. The value of bed rest early in the course of the common cold and its secondary cough is illustrated by the observation that it may cause a cough to subside and sometimes disappear completely. The atmospheric environment should be moist and moderately warm. Such air usually soothes the impulse to cough, whereas hot dry air may provoke and prolong the cough. Humidification of air can be achieved in several ways: by means of evaporating pans filled with water placed over steam radiators, by means of steam kettles, or by the use of inhalation apparatus. Excellent results are obtained in a bedroom that adjoins a bathroom. The shower is permitted to run for about an hour, and the resultant steam disseminates rapidly throughout the adjoining room.

Medicinal treatment of coughing has long been popular. Although a sedative effect is frequently desirable, it is highly advisable to utilize sedation with discrimination. Expectorants, which assist in the removal of exudate from the respiratory tract, accomplish their purpose by stimulating the cilia to remove secretions and by thinning the secretions to lower their viscosity. Opiates and atropine increase viscosity and adhesiveness, thereby adding to the difficulty of the effective expulsion of secretions. It has been demonstrated that cilia are capable of removing overlying secretions in a comparatively short time. The rate of transit is twice as rapid when the trachea is in the horizontal position as when it is in the vertical position. This phenomenon contributes some validity to the concept of bed rest. Effective expectorants, which function either by activating cilia or decreasing secretion viscosity, include ammonium chloride, sodium citrate, ammonium carbonate, and volatile oils of turpentine, anise, pine, lemon, and eucalyptus. Ammonium chloride is useful in a cough characterized by scanty or tenacious sputum, a feature often observed in acute and subacute inflammation of the upper respiratory tract. The preparation of the cough mixture should be governed by the type of cough and the age of the patient. In the case of an unusually severe cough, antibiotics and the sulfonamides may be employed effectively, with suitable observation.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any official bodies unless specifically stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

DIET IN CORONARY DISEASE

TO THE EDITOR:—*I would like an authoritative appraisal of the dietary management of coronary atherosclerosis. A patient had an occlusion (anterior branch) followed by myocardial infarction 16 months ago. He hopes to put in a few more years of useful work. The information I have regarding a proper diet is confusing. A trial of the low fat, low cholesterol type of diet resulted in a rise of his blood cholesterol level from 250 to 314 mg. per 100 cc. after 30 days. His blood pressure averages about 130/95 mm. Hg. His age is 60. He feels better when on a diet high in protein and moderately low in fat and carbohydrates.* *M.D., California.*

ANSWER.—The feeling of confusion expressed about the best diet for use in the prevention and treatment of coronary heart disease is shared by the great majority of physicians of this country, including many authorities on the subject. Dogmatic statements about any routine diet that can be advised for general use lack confirmation, although eventually, after some years of further study, much more will doubtless be known as to the best diets for various types and kinds of both sick and healthy persons. It is unlikely that any uniform diet routine for everyone can ever be advised.

At present, it would seem reasonable to advise such a diet as that mentioned, namely, one fairly high in protein and moderately low in fats and carbohydrates, even if there were some unusual disease background, such as familial hypercholesterolemia or diabetes. To omit fats altogether, or even to omit the dairy products only, may actually not be necessary for a person who already has coronary heart disease or who is a candidate for it. It may be more important to restrict total caloric intake so that there will be no gain in weight or actually some weight reduction if there is obesity. The internal production of cholesterol by the human body may prove to be just as important as, or even more important than, the ingestion of cholesterol. Thus, it seems sensible to practice moderation in the diet and to await further and more conclusive evidence than we have today.

HYPERTENSIVE RETINOPATHY

TO THE EDITOR:—*What is the present concept of the different grades of hypertensive retinopathy as seen with the ophthalmoscope? What is the characteristic appearance of arteriosclerotic retinopathy? What appearance of the ocular fundus enables one to differentiate the changes of vascular spasm from those of vascular sclerosis?* *M.D., Pennsylvania.*

ANSWER.—Wagener, Clay, and Gipner (Classification of Retinal Lesions in Presence of Vascular Hypertension, *Tr. Am. Ophth. Soc.* **45**:57, 1947) recognize three distinct types of alteration of the retinal arterioles in different phases of hypertensive disease. These changes are each divided into four grades:

A. Generalized narrowing (which probably represents increased tone of the arteriolar system): Grade 1. Reduction of caliber of arterioles to ¾ of average caliber or to ½ of caliber of veins. Grade 2. Reduction of caliber of arterioles to ½ of average caliber or to ⅓ of caliber of veins. Grade 3. Reduction of caliber of arterioles to ⅓ of average caliber or to ¼ of caliber of veins. Grade 4. Arterioles thread-like or invisible.

B. Generalized arteriole sclerosis (organic thickening of arteriole wall): Grade 1. Brightening or increased luster of the arterioles; mild depression of the veins at the points of arteriolar crossing, with reduction in visibility of those portions of the veins that underlie the crossing arterioles. Grade 2. Burnished coppery color of the arterioles, with definite depression of underlying veins, widening of the apparent arteriolovenous crossing spaces, and almost complete invisibility of those portions of the veins that underlie the crossing arterioles. Grade 3. Polished silver color of the arterioles and widening of the apparent arteriolovenous crossing spaces, with a change in the course of

the veins (right-angled crossing), complete invisibility of those portions of the veins that underlie the crossing arterioles, and distal dilation of the veins. Grade 4. Arterioles visible only as fibrous cords, with no circulating blood.

C. Focal constriction (spasm) or focal sclerosis of arterioles: Grade 1. Localized narrowing to ⅔ of the caliber of proximal segment of arteriole. Grade 2. Localized narrowing to ½ of the caliber of proximal segment of arteriole. Grade 3. Localized narrowing to ⅓ of the caliber of proximal segment of arteriole. Grade 4. Arteriole invisible beyond point of constriction.

These authorities recommend that the terms "arteriosclerotic retinopathy" and "arteriolosclerotic retinopathy" be dropped, since the lesions usually so designated (punctate hemorrhages and punctate white areas) are likely to be end results of either venous occlusion or hypertensive retinopathy and at times are of diabetic origin. An accurate differential diagnosis with these possibilities in mind is preferable to their inclusion under some substantive term to which is attached the adjective "arteriolosclerotic." Pure vascular spasm, uncomplicated by vascular sclerosis, is best observed in toxemia of pregnancy or in severe acute hypertension. The arterioles are generally narrowed, and there are segments of focal constriction. In later stages there is edema of the retina and, usually, of the optic disk, cotton wool patches and hemorrhages. In vascular sclerosis there may be decreased transparency of the arteriole wall, with increased luster of the vessel wall and visible thickening. There may be changes in the arteriolovenous crossing.

INGUINAL HERNIA

To the Editor:—*A white man, 68 years of age, has an incomplete inguinal hernia on one side. What results may be anticipated with sclerosing injections?*

M.D., New York.

Answer.—The treatment of hernia is still surgical. No permanent results can be expected with sclerosing injections. An inguinal hernia occurs when a long-standing hernial sac becomes dilated and fills with abdominal viscera because of developing weakness in the abdominal wall. Such a condition responds only to surgical repair consisting of removal of the sac followed by the strengthening of the abdominal wall. Today, a man of 68 is a relatively young man, and he should have the benefit of operative treatment. Many patients 10 or more years older have had successful operative repair of their hernias, with almost no mortality and a high percentage of cures.

GIRL GROWS EIGHT INCHES IN YEAR

To the Editor:—*A girl, 14½ years of age, has grown 8 in. (20.32 cm.) in the past year. Her height now is 6 ft. ¾ in. (184.79 cm.) and her weight, 130 lb. (59 kg.). She menstruated the first and only time at age 14¼. This period lasted about 5 days. Her breasts are fairly well developed, and the pubic and axillary hair development is about average. Her skin, hair, and nails are about average. At birth she weighed 7½ lb. (3.43 kg.) and her dentition, walking, and talking occurred at about the average age. Her mother is 5 ft. 8 in. (172.72 cm.) tall, and her father is 5 ft. 11½ in. (181.61 cm.) tall. The mother has heard of some kind of injection that will stop further growth of children. Is this possible?*

M.D., California.

Answer.—The main problem is whether the patient is a pituitary giant. Some additional information may be obtained by roentgenographic examination of the sella turcica and of various epiphyses, such as those of the right elbow, right knee, and both hands. If the epiphyses are open, further growth will occur. If they are closed, growth is about complete. It is not clear how much time has elapsed since her first menstrual period. Irregularity of menstruation would indicate some pituitary disturbance. Growth of 8 in. (20.32 cm.) in a single year is unusual at puberty but is observed in rare instances with no overproduction of growth hormone. If the patient is a normal girl who has inherited the quality of tallness, no treatment is indicated. If she is a pituitary giant, then an attempt may be made to inhibit production of growth hormone either with large doses of estrogen or with roentgen ray therapy directed over the pituitary.

PAIN IN ARM

To the Editor:—*A woman, aged 70, had bursitis of the right shoulder two months ago. It was not severe but was followed by pain in the anterior aspect of the arm, between the shoulder and elbow, with and without movement. She now has severe pain when adjusting her hair at back of her head and cannot get her hand back to the sacral region. Roentgenograms of the chest and arm are normal. She has had salicylates, deep x-ray therapy (six doses), and cortisone, 200 mg. daily for three days and then 100 mg. daily for four days. The diagnosis by a colleague was tenosynovitis, and he advised heat therapy and stretching exercises. We were advised that it may take months for the condition to clear up, but the patient is reluctant to take an anesthetic for the stretching. Please advise any further diagnostic means and any other treatment. The patient is in good health; her blood pressure is 140/84 mm. Hg, the urine is normal, and the heart and lungs are normal clinically and roentgenographically.* *M.D., New York.*

Answer.—Are you sure this condition is bursitis? Roentgenograms should be made of the patient's neck, as the cause of the pain in the arm could be nerve root irritation secondary to degenerative changes in the cervical intervertebral disks. Such pain will cause a patient to keep the arm relatively immobile so that periarticular fibrosis will subsequently cause the limitation of motion that you describe. Manipulation of such a shoulder with anesthesia in a 70-year-old person is considered somewhat risky, as the osteoporosis caused by senescence and immobilization may predispose to a fracture of the humerus during the manipulative procedure. If the primary difficulty is in the shoulder, hot packs, massage, and gentle stretching within the limitation of the patient's tolerance will suffice. It is true that this lesion may take a long time to clear, but in general the prognosis for a return of good function is excellent.

AUREOMYCIN AND DIARRHEA

To the Editor:—*A patient was treated for virus pneumonia with 500 mg. aureomycin initially, then 250 mg. every 6 hours for the next eight doses. A mild diarrhea developed, with tenesmus, made worse by bulky and rough foods and only partially and temporarily relieved by ingestion of more aureomycin. This has lasted for 15 months. Was aureomycin the cause of the diarrhea in this case? What is to be done to break the vicious circle, if one exists?* *M.D., California.*

Answer.—It is difficult to determine from the facts given whether aureomycin is the cause of the diarrhea. With the patient completely off the drug a thorough investigation should be made and should include proctoscopic and roentgenographic examination. Some of these patients seem to respond to the administration of folic acid and vitamin B_{12}; this therapy should certainly be tried rather than continued treatment with the antibiotic.

LIPODYSTROPHY

To the Editor:—*Is corticotropin (ACTH) therapy or any other treatment of value in lipodystrophy of the childhood type, characterized by absence of fat on the upper part of the body?*

M.D., Alabama.

This inquiry was referred to two consultants, whose respective replies follow.—Ed.

Answer.—Just as there has been no satisfactory explanation for the occurrence of lipodystrophy, there has been no therapy to date that is of any value. Although corticotropin has not been used specifically in this disease, there is no reason to suppose that it would be of value.

Answer.—No treatment has been found to be of value in progressive lipodystrophy. The effect of corticotropin or cortisone on this disease has not yet been reported.